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WEIL'S DISEASE IN THE UNITED STATES*

Report of a Case in Connecticut

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NEW HAVEN, CONNECTICUT

IN 1935, Jeghers, Houghton and Foley[1] reported the first established case of Weil's disease from New England, reviewed the literature concerning leptospirosis and summarized the data concerning 11 previous sporadic cases that had been reported from various parts of the United States, including 4 from New York,[2–4] 1 from New Jersey,[5] 2 from Pennsylvania,[5, 6] 1 from the District of Columbia,[7] 1 from Virginia[8] and 2 from California.[9] In all but 2 of the reported cases the correctness of the clinical diagnosis appears to have been well supported by the successful transmission of leptospiral infection to guinea pigs with blood (4 cases), urine (3 cases), spinal fluid (1 case) or kidney tissue (1 case), or by the satisfactory microscopic demonstration of leptospirae in tissues obtained at autopsy (3 cases). In 1 case[5] confirmation of the diagnosis was based solely on the demonstration of "a few typical parasites" in dark-field examination of the blood on the tenth day of the disease, while in 1 case,[9] concerning which there may be some doubt, occasional spiral forms, which were described as appearing more like spirilla than leptospirae, were seen in sections of the kidney stained by Levaditi's method.

Since 1935, sporadic cases have been recorded with increasing frequency. In 5 of these, from Virginia,[10] Michigan,[11] New York[12, 13] and New Jersey,[14] the diagnosis seems to have been adequately supported by confirmatory laboratory tests, namely, successful transmission of the infection to guinea pigs in 4 cases, with additional demonstration of *Leptospira icterohaemorrhagiae* at autopsy in 2, and the development of specific agglutinins to a titer of 1:30,000 in 2. In addition to these 5 fully documented cases, 11, all from California, are incidentally referred to by Meyer, Stewart–Anderson and Eddie,[15] and 1 from Rochester, New York,§ is cited by Syverton, Stiles and Berry.[16] Seven cases have been reported from Colorado,[17] but the apparent ease with which numerous leptospirae were supposedly seen in dark-field examinations of the blood for long periods of time is so inconsistent with usual experience as to cast doubt on the validity of the diagnoses. Concerning the remaining 7 cases reported, 3 from Texas[18] and 4 from Rhode Island,[19] the data presented are so limited that evaluation is difficult.

The case reported here appears to be the first recorded from Connecticut.

CASE REPORT

A 29-year-old dairyman, of Wallingford, Connecticut, previously well, was suddenly seized on the afternoon of November 11, 1939, with pain in the calves of both legs, weakness and dizziness. During the evening he became progressively sicker, with chills, fever and headache. About midnight his neck became stiff and painful. He was severely nauseated and vomited frequently. He was seen by his physician, Dr. Charles A. Breck, early on the morning of November 12 and was referred to the Meriden Hospital.‡

At physical examination on admission the patient appeared acutely ill, bathed in perspiration, pale, weak and apprehensive. The conjunctivas were injected, the lips were dry, and the tongue was dry and coated. The neck was slightly stiff and painful. The lungs showed a few moist rales at the left base posteriorly. The blood pressure was 96/68. There was slight tenderness of the abdominal muscles. The liver and spleen were not felt. All deep reflexes were slightly hyperactive. The abdominal reflexes were lacking; the Kernig test was negative. The temperature was 102.6°F., the pulse 90, and the respirations 20. There were no other abnormal findings.

The white-cell count was 27,350, with 96 per cent polymorphonuclear neutrophils (nonfilament, 57 per cent; filament, 39 per cent) and 4 per cent lymphocytes. The urine was amber-colored, slightly cloudy and acid, with a specific gravity of 1.014. It showed no albumin or

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§In addition to this, other cases, not yet reported, have occurred in Rochester, New York (Berry, G. P.: personal communication).

‡I am indebted to Drs. T. P. Murdock and J. A. Wilson, of Meriden, and Dr. C. A. Breck, of Wallingford, for making available the clinical record of this case prior to admission to the New Haven Hospital.

sugar. The sediment contained numerous epithelial cells. A Kline test was negative. The nonprotein nitrogen of the blood was 36 mg. per 100 cc., and the blood sugar 107 mg. X-ray examination of the chest was negative. A lumbar puncture showed an initial pressure of approximately 250 mm. of water. Ten cubic centimeters of clear spinal fluid was withdrawn; the fluid had a cell count of 30 per cubic millimeter, mostly red blood cells; a Pandy test was negative; a stained smear contained no organisms and rare lymphocytes; a culture showed no growth. Blood cultures showed no growth. Agglutination tests for typhoid and paratyphoid fevers and brucellosis were negative.

The subsequent course of the illness is shown in Figure 1. The predominant symptoms during the first 4 days were prostration, fever, headache, meningismus and severe myalgia, principally in the neck, back and legs. On the 3rd day epistaxes began, recurring at intervals until the 13th day. A second lumbar puncture on the 4th day revealed a clear spinal fluid under normal pressure with 80 red blood cells per cubic millimeter. On the 5th day moderate jaundice developed; it lasted about a week. The liver became palpable and tender. The spleen was not palpable. With the jaundice there were severe nausea and vomiting, the vomitus on the 7th and 8th days containing blood. Evidence of renal involvement was negligible. From the 10th day on the patient steadily improved, the temperature reaching normal by the end of the 2nd week. He was discharged on the 19th day for further convalescence at home, no diagnosis having been established.

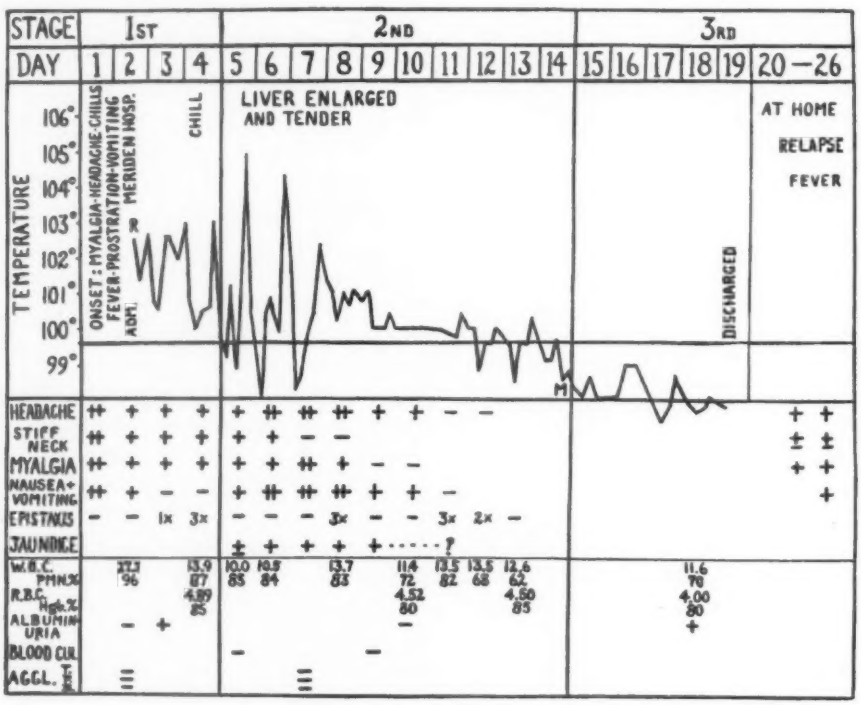

FIGURE 1. *Early Clinical Course of Patient with Weil's Disease at the Meriden Hospital. Agglutinins:* T — *typhoid bacilli;* P — *paratyphoid A and B bacilli;* B — *brucella organisms.*

After returning home the patient again developed moderate headache and soreness in the legs. His appetite was poor, and he felt drowsy and somewhat feverish. His vision seemed slightly blurred, and he vomited on two occasions. On December 12, the 27th day of his illness, he was admitted to the New Haven Hospital for further study. Except for an elevated temperature, slight stiffness of the neck, a palpable liver extending 1.0 cm. below the right costal margin and some muscular soreness on flexion of the legs, the physical examination revealed nothing abnormal. The results of laboratory and other special examinations and the subsequent course of the illness are shown in Figure 2. The patient was discharged improved on December 18.

A few days after admission, review of the clinical course of the illness clearly suggested Weil's disease. The patient stated that about 10 days before the onset of his disease he had been engaged in tearing down an old barn which was swarming with rats. Dark-field examination of the urinary sediment on the 33rd and 34th days of the disease, possibly too late for a positive result, failed to reveal leptospirae, but samples of blood serum collected on the 38th and 47th days and submitted to the National Institute of Health in Washington, D. C., were reported to show complete agglutination with Type 1 *L. icterohaemorrhagiae* to a dilution of 1:10,000 and 1:30,000, respectively. Positive agglutination at these titers is considered diagnostic of leptospiral infection.[20] Taken in conjunction with the history of exposure to rats, an appropriate incubation period and the typical course of the illness with its three characteristic stages, the positive agglutination tests, with a rising titer between the 38th and 47th days, seem adequate to establish the diagnosis of Weil's disease.

The exact incidence of Weil's disease in the United States is uncertain, although the increas-

ing frequency with which cases are recognized suggests that it may be more prevalent than is generally supposed. That there is a large reservoir of *L. icterohaemorrhagiae* in the rat population has been well established through numerous surveys.[2, 15, 16, 21] It is likewise well established that the carrier rat which contaminates its environment by excreting leptospirae in its urine is the usual source of infection for man. Under these circumstances it is not surprising that the well-authenticated cases that have been reported in this country have all been sporadic, and with 3 exceptions have occurred in men, many of whom were known to have lived or worked in places infested with rats. Of the exceptions 1 patient was a woman accidentally infected in the laboratory,[2] 1 a young child stated to have contracted the infection from a pet dog sick with leptospirosis[11] and 1 a schoolboy living in a rat-infested shack and engaged for several months in trapping rats.[14]

The susceptibility of dogs to infection with *L. icterohaemorrhagiae* through contact with rats and the possibility that the dog may on occasion act as an intermediate vector between rat and man have received considerable attention,[20, 22, 23] and are illustrated by the case reported by Martmer.[11] This series of events should not, however, be confused with true canine leptospirosis,[24] a disease of older dogs caused by *L. canicola,* an organism which is not found in rats, and which, unlike *L. icterohaemorrhagiae,* possesses but little virulence for guinea pigs.[22] That man may be infected with *L. canicola,* as well as with *L. icterohaemorrhagiae,* is now well established, particularly through the studies of Schüffner[20] in Holland, where human canicola fever has been shown to occur. It seems not improbable that the same is true of this country, for Meyer, Eddie and Stewart-Anderson[15, 22] have already demonstrated that canine leptospirosis is prevalent in California, and have cited a case of human infection with *L. canicola* in a veterinarian's assistant at Stockton.

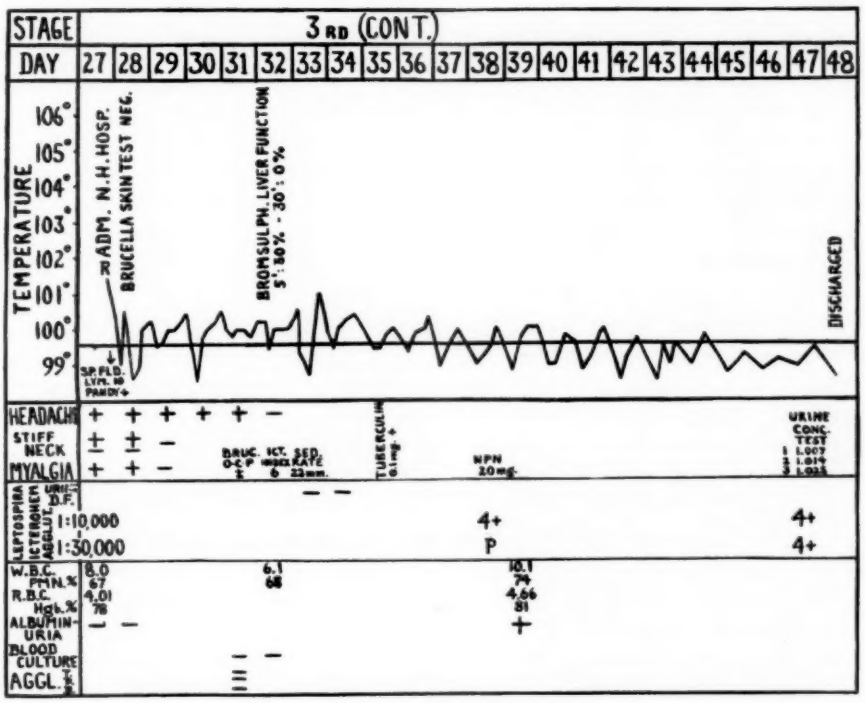

FIGURE 2. *Further Clinical Course at the New Haven Hospital. D.F. — dark-field examination; O-C-P — opsonocytophagic index.*

A clinical diagnosis of Weil's disease may doubtless be readily suspected in an otherwise obscure infection after the onset of the second stage of the disease with jaundice, hemorrhage and evidence of renal damage, particularly if the patient is a sewer worker,[25] fish handler,[26] slaughterhouse worker or miner, or is known to live or work in rat-infested premises or to have fallen into polluted water.[20] Overemphasis on the symptomatology of the second stage of the disease, however, especially the icteric and hemorrhagic features, which in many cases may be quite minor or even lacking,[20] should yield place to a greater emphasis on the characteristics of the first stage, if earlier diagnosis and more frequent recognition of Weil's disease are to be accomplished. These character-

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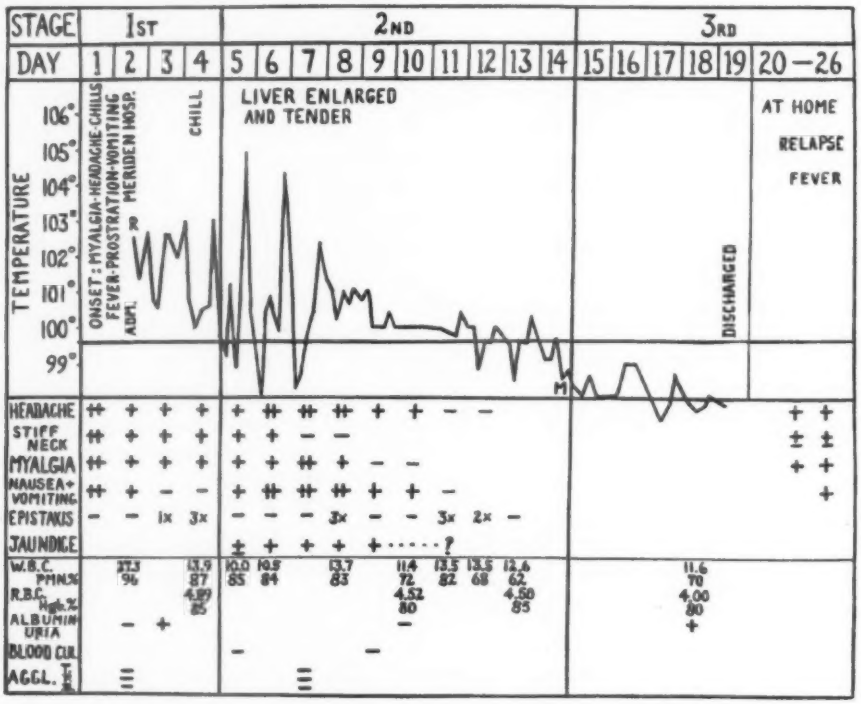

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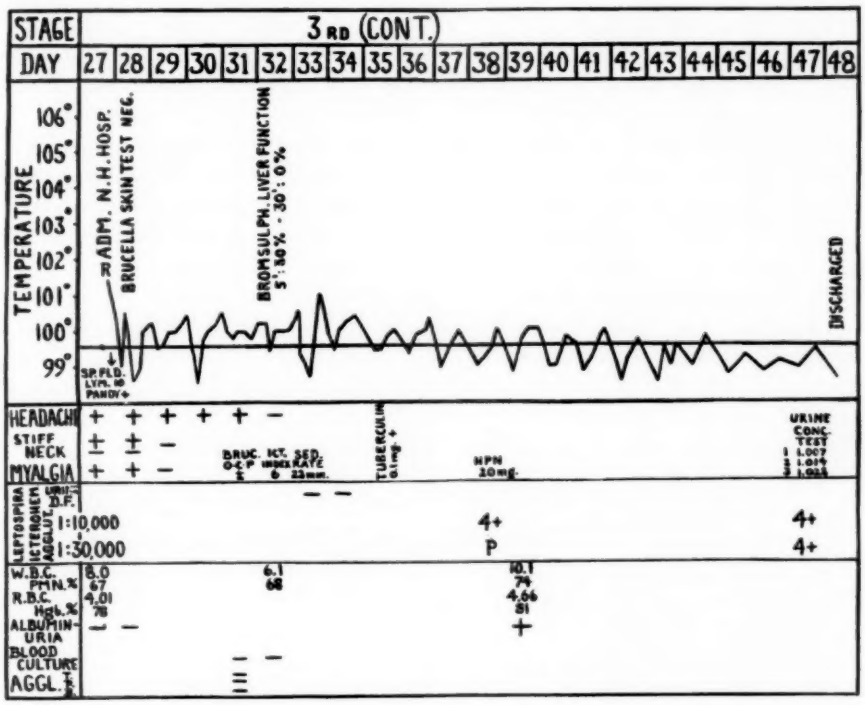

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istics are well illustrated by the case reported here, namely, abrupt onset with severe myalgia, particularly in the calves but also in other muscles, promptly followed by chills, fever, headache, nausea and vomiting, and suggestive symptoms and signs of meningeal irritation. Conjunctival injection is often a conspicuous feature. Herpes and hiccoughing may be present. Further than this, physical examination will add little. There will be a polymorphonuclear leukocytosis, with an increase in the proportion of immature cells. Other ordinary laboratory examinations are of little value in differential diagnosis.

While the foregoing group of symptoms is common at the onset of many severe acute infections, their persistence for two or three days without the development of further evidence of some well-recognized infectious disease might well lead to a suspicion of Weil's disease. Questioning a possible source of infection and a search for leptospirae in the blood and spinal fluid by dark-field examination, culture and guinea-pig inoculation, at a time when they are still present and most readily recoverable, would then be indicated. Subsequent confirmation of the diagnosis in a suspected case may be sought by dark-field examination and guinea-pig inoculation of the centrifuged sediment from 50 cc. of freshly passed urine* from the sixth to the thirtieth day of the disease, and by serum agglutinin tests after the tenth day. Biopsy of the gastrocnemius muscle may be of value. Vacuolation, swelling, loss of striations and hyalinization of isolated or groups of adjacent muscle fibers and infiltration with histiocytes, polymorphonuclear leukocytes and plasma cells may be seen on microscopic examination.[1] Of the laboratory procedures available, animal inoculation, blood cultures and serological tests appear to be the most reliable, and dark-field examination of the blood and urine the least satisfactory and most difficult.[24] The agglutination test requires experience. For this reason, samples of serum should be submitted to a laboratory thoroughly familiar with the technic, such as the National Institute of Health.

It has often been suggested that epidemic infectious jaundice, outbreaks of which occur with considerable frequency in this country, may be of leptospiral etiology and represent a relatively mild, epidemic form of Weil's disease. No evidence substantiating this view, however, had been adduced up to 1923,[27] nor have more recent efforts[28, 29] to isolate leptospirae from patients with epidemic jaundice been successful. Although Slesinger and Zeligman[29] recorded that the National Institute of Health had reported positive agglutination reactions against *L. icterohaemorrhagiae,* with several specimens of convalescent blood from both jaundiced and non-jaundiced cases in the epidemic studied by them in Windber, Pennsylvania, it is their opinion that the cases were the usual type of epidemic infectious jaundice and not Weil's disease.[30]

Up to the present at least, the epidemiologic and certain of the clinical characteristics of Weil's disease, as it has occurred in this country, have been quite distinct from those of epidemic infectious jaundice. The former has been recognized only as a sporadic disease occurring almost solely in adult men, while the latter commonly occurs in familial, institutional and community epidemics and largely among children, adolescents and young adults of both sexes.[27] The severe symptoms of the hemorrhagic and renal phenomena of the second stage of Weil's disease are, at most, quite rare in epidemic infectious jaundice. The polymorphonuclear leukocytosis of Weil's disease is also usually lacking in epidemic jaundice, which commonly exhibits a normal or somewhat low white-cell count, not infrequently with a relative lymphocytosis. In view of these contrasts it would seem appropriate to regard the two diseases as distinct until the etiology of epidemic infectious jaundice has been determined. Sporadic cases of so-called catarrhal jaundice, which clinically closely resemble individual cases of epidemic infectious jaundice, might perhaps be regarded with more suspicion as possible cases of mild leptospirosis, but here again evidence is wanting and further study is needed.

How often the more frequent consideration of Weil's disease as a possible diagnosis and the application of appropriate diagnostic procedures will prove fruitful is, of course, impossible to predict. At least they may serve to determine whether sporadic cases of leptospirosis are as prevalent in this country as they appear to be in Great Britain[25, 26] and elsewhere in Europe.[20]

Summary

A case of Weil's disease in Connecticut is reported. The occurrence of the disease in the United States is briefly reviewed. The more frequent recognition and diagnosis of Weil's disease would appear to depend on a wider appreciation of its prevalence, a greater familiarity with its clinical symptomatology, particularly that of the initial pre-icteric stage, and a more frequent use of laboratory tests of proved diagnostic value at appropriate stages of the infection.

*Centrifugation is practically useless unless an angle centrifuge and high speeds are used. It is essential that the urine have an alkaline or at least a neutral reaction (Berry, G. P.: personal communication).

Since the preparation of this report 7 additional cases in or near Detroit, Michigan, have been recorded.[31] Four of these occurred in men and 3 in persons in their teens, 1 of whom was a girl of fourteen. Three of the adults were poultry dressers.

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ADVANCES IN THE ROENTGEN-RAY TREATMENT OF TUMORS OF THE BLADDER*

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IN THE spring of 1937, a roentgen-ray therapy unit operating at from 1000 to 1200 kv., constant potential, was put in operation at the Collis P. Huntington Memorial Hospital in Boston. This apparatus has since been used chiefly for the treatment of deep-seated malignancies. The routine setting for such treatment is 70-cm. distance and a filter of 3.5 mm. of lead plus 8 mm. of copper. When a gold anode is employed, the output is 80 r per minute per milliampere of current. The average wave length of the radiation obtained is essentially that derived from a radium applicator filtered with the equivalent of 2 mm. of lead. The quantity of radiation is equal to that which might be obtained from about 2000 gm. of radium.

The advantages of this type of radiation are fourfold. Because of the high intensity it becomes feasible to use a long target-to-skin distance, thereby increasing the depth dose. Approximately 50 per cent of the radiation delivered at the surface reaches the center of the average-sized pelvis. There is a greater tolerance of the skin as compared with the usual 200-kv. rays. This has not only been observed in human beings but has been demonstrated experimentally in animals. The amount of radiation reaching deeply is very little affected by the size of the portal of entry. It is therefore possible to use smaller fields covering only the disease-bearing area without having to resort to large portals to increase the depth dose. With small portals of entry, the amount of scattered radiation is about one third of that produced at 200 kv. This results in a lessened general reaction (roentgen sickness) on the part of the patient.

The skin reaction is generally the limiting factor in the treatment of deep-seated neoplasms with 200-kv. rays. The reverse, however, is true with supervoltage radiation. There is no longer a question of damage to the superficial structures,

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but the dosage is limited by the tolerance of the deep tissues, such as the intestines, bladder and so forth.

In view of the fact that radiation damage may not become manifest until several years after treatment has been concluded, it has seemed to us advisable to proceed with caution. A routine preliminary series of treatments for carcinoma of the bladder, consisting of 200 r delivered to each of three pelvic portals, 12 by 12 cm., one front and two posterior oblique, has been established. This is frequently augmented by 600 r to each of two lateral portals. Treatment is administered at the rate of 400 r per day. During the third week most patients experience diarrhea with increased vesical irritation. There is remarkably little roentgen sickness, and other than the bladder and bowel complaints, most patients experience little reaction. A month after the treatment has been concluded the patients are cystoscoped, and if the tumor has regressed, further radiation is instituted. The amount of radiation given in the second series is dependent on the general condition of the patient and the response of the tumor. We have not yet determined the maximum dosage which it is safe to give. We have been impressed with the dearth of untoward reactions in normal structures, and it seems likely that doses much greater than we have thus far employed will eventually be considered justifiable. As one of us (R. D.[1]) has pointed out in an earlier communication, the amount of radiation administered in the preliminary series is not sufficiently large to ensure permanent control of carcinoma of the bladder.

Thirty-five patients with tumors of the bladder have been treated during the last three years at this clinic with the 1000-kv. roentgen-ray unit. Although the number of cases is small, these patients have been carefully studied and biopsies of the tumors have been taken before treatment in practically every case. Additional tissue has been removed from the tumors during and after treatment insofar as possible. Frequent cystoscopic examinations have served as an aid in determining radio-sensitivity and regression or disappearance of these new growths. The general condition of the patients and their ability to tolerate large amounts of external radiation have been determined by frequent physical examinations, blood counts and a follow-up routine.

We believe that supervoltage radiation differs sufficiently from other methods of treating tumors of the bladder to require a separate evaluation. Results so far seem to warrant its continuation, although supervoltage radiation is still in the experimental stage and its end results probably cannot be fairly evaluated for several years. Its value, we believe, should be considered at present not so much a means of curing cancer of the bladder as an agent which causes regression of the tumor and alleviates symptoms. With this point of view, so recent and untried an agent may be fairly evaluated.

As stated elsewhere, we[2] believe that localized tumors of the bladder are best treated by radical removal through excision, or destruction and implantation of radium. Supervoltage radiation has been used only to treat patients with extensive malignant tumors, unsuited to surgery, or those too feeble to stand operation. The patients included in this report, therefore, are chiefly debilitated individuals with advanced inoperable cancer. They have averaged sixty-two years of age.

Before starting supervoltage treatments tumor tissue has been obtained by biopsy or at operation in every case but 1. The exception was a huge infiltrating tumor of the bladder, obviously malignant. These tumors were classified according to the Tumor Registry of the American Urological Association* as shown in Table 1.

TABLE 1. *Classification of Tumors of the Bladder.*

TYPE	NO. OF CASES	PER CENT
Papillary carcinoma, Grade I	3	9
Papillary and infiltrating carcinoma, Grade II *a*	17	49
Infiltrating carcinoma, Grade II *b*	6	17
Nonpapillary infiltrating carcinoma, Grade III	6	17
Sarcoma	1	3
Ungraded	2	6
Total	35	

The papillary infiltrating type of growth was the commonest in this series, although nonpapillary infiltrating tumors comprised about one third of the cases.

Biopsies have been a valuable aid, although disappointing in some respects. In several cases of obviously malignant neoplasms the report from the first biopsy was "chronic inflammation." On the other hand, tissue removed from areas grossly but not frankly neoplastic sometimes contained actively growing tumor cells. This was particularly

*The official basis of grading is as follows:

Grade I. Papillary carcinoma: all papillary tumors in which there is no clinical evidence of infiltration, and in which no obvious infiltration of the pedicle or bladder wall can be demonstrated on histopathological examination; most of the cells are typical in appearance or arrangement.

Grade II. *a*. Papillary and infiltrating carcinoma: obviously infiltrating papillary tumors and carcinomas in which the papillary structure is recognizable but most of the cells are atypical in appearance and arrangement. *b*. Infiltrating carcinoma: nonpapillary squamous-cell carcinomas in which the cells are fairly uniform in size and type or have a tendency to form keratohyaline and epithelial pearls.

Grade III. Nonpapillary infiltrating carcinoma: very anaplastic, infiltrating carcinomas; practically all the cells atypical in appearance; very slight or no differentiation.

true among patients whose tumors disappeared as a result of radiation, and here a positive biopsy report demonstrated the need for further treatment. Biopsy, however, proved disappointing as an indication of the radio-sensitivity of tumors, although further study of the correlation of histology and radio-sensitivity would be helpful. Biopsy was useful in establishing a diagnosis of papillary carcinoma, Grade I, since such tumors responded slightly, if any, to external radiation. Our experience in this respect has paralleled that of tumors

TABLE 2. *Individual Dosage.*

PATIENT	AGE	DOSAGE	PATIENT	AGE	DOSAGE
	yr.	r		yr.	r
T. B.	83	8,400	F. K.	60	8,400
F. S. B.	80	6,000	G. M.	58	20,800
W. B.	48	8,400	W. M. A.	47	13,200
Z. B.	57	13,900	P. M. C.	62	10,200
A. B. C.	63	14,900	J. M. E.	73	6,000
A. M. C.	77	12,800	J. M. K.	58	10,600
M. C.	69	12,000	J. N.	75	9,600
C. L. C.	74	17,300	C. P.	62	7,200
J. E. C.	63	6,000	C. A. P.	64	12,000
T. D.	58	6,400	A. S.	62	7,600
R. T. E.	82	12,000	A. S.	46	13,600
H. F.	74	22,200	A. S.	52	12,000
J. F.	73	10,000	M. S.	35	6,000
J. G.	34	4,200	S. T.	44	10,200
A. G.	68	12,400	G. T.	78	6,000
L. R. H.	59	12,400	I. T.	59	6,800
F. H.	77	7,700	N. V.	33	6,400
R. H.	73	7,200			

of other organs: the less differentiated the cell type, the more radio-sensitive the tumor. Except for this generalization, however, it has not been possible to gauge radio-sensitivity from the histological examination of biopsied specimens.

Table 2 shows the individual dosage given in this series of cases.

Our experience regarding the response of the different types of bladder neoplasm to radiation is summarized in Table 3. As a result of treatment, over half of these tumors regressed, that is, were reduced by at least one third. Gross disappearance, as determined by cystoscopic examination, occurred in about one third of the cases. Frequently, however, the disappearance was only temporary and recurrence was obvious in a few weeks or months. The effects of radiation seemed more marked on the intravesical portions of these tumors than on the parts that had deeply invaded the bladder wall. In many cases induration of the bladder wall persisted and was readily detected by rectal or vaginal examination. Biopsies were positive in a number of such cases, although, otherwise, frank tumor could not be identified.

The tumors most sensitive to radiation were the rapidly growing neoplasms with little or no cell differentiation, the infiltrating Grade III carcinomas. Over 80 per cent of such growths regressed, sometimes to an astonishing degree, and over 60 per cent disappeared, at least for a time. Such tumors were likely to recur rapidly, however, and in none has there been evidence of prolonged permanent cure.

With tumors of moderate malignancy, the papillary and nonpapillary types of growth were about equally radio-sensitive. The chance that such tumors may respond favorably to this form of radiation appears to be good, since there was regression in over 60 per cent of our cases. Gross disappearance occurred in about one third of these growths. It is doubtful if any cases were cured by radiation alone, although in a few sufficient regression resulted to allow transurethral removal of the remaining tumor and radium implantation. Several cases so treated have remained free of tumor long enough so that the chances of cure are excellent.

Epithelial tumors of the lowest grade of malignancy, the benign papillary type, responded poorly to radiation. The 3 cases reported were huge tumors which filled most of the bladder cavity but histologically were papillomas. One such growth, composed of very delicate, long papillary projections, disappeared except for a few small nubbins which were easily, and probably permanently, destroyed by transurethral fulguration. No effect other than the control of bleeding was as a rule obtained in tumors of this type by supervoltage treatment. External radiation may be useful even in this group, however, to stop persistent bleeding and to improve the patient's condition enough to stand open operation.

TABLE 3. *Response of Types of Bladder Neoplasm to Radiation.*

TYPE OF TUMOR	NO. OF CASES	REGRESSION OF TUMOR		GROSS DISAPPEARANCE OF TUMOR	
		NO. OF CASES	PER CENT	NO. OF CASES	PER CENT
Grade I	3	1	33	0	0
Grade II *a*	17	11	64	5	29
Grade II *b*	6	4	66	3	50
Grade III	6	5	83	4	66
Sarcoma	1	0	0	0	0
Ungraded	2	0	0	0	0
Totals.....	35	21		12	
Average percentages			60		34

One case of sarcoma of the bladder was not benefited by external radiation. This tumor was either leiomyosarcoma or rhabdomyosarcoma.

Bleeding or frequent and painful urination was relieved in over half the cases. Such relief was frequently only temporary, and symptoms returned with extension or reappearance of the growth. An occasional patient was made worse by treatment.

Conclusions

Roentgen rays produced at 1000 kv., constant potential, afford a means of delivering to deep-seated neoplasms doses which are limited not by skin effect but by the tolerance of underlying structures. The results that we have obtained in radiating bladder tumors during the last three years with rays produced at this high potential are definitely superior to those we have observed in treating similar tumors with rays produced at lower voltages. Well-marked regression of the growth was obtained in about half the cases, with at least temporary disappearance of the lesion in about a third. Pain and bleeding were relieved in approximately half the cases. It is our belief that as we gain experience with this type of radiation these results will improve.

Emphasis must be laid on the fact that this method is not a substitute for surgery. Tumors suitable for excision or resection should be handled by operation.

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THE RIB JOINTS

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There are twenty-four joints, called the costovertebral joints, formed by the conjunction of the heads of the ribs with the sides of the spine. Besides these, there are twenty joints, called the costotransverse joints, formed by the angles of the ribs and the outer parts of the transverse processes of the upper ten dorsal vertebrae. This makes forty-four joints involved in the mechanism of the thorax, each being a true joint and capable of disease or injury as would be true with other joints, with the added disadvantage that while most of the others have periods of rest after periods of activity the rib joints, unless they become ankylosed from disease, never rest entirely so long as life exists.

The costovertebral joints of the upper ten dorsal vertebrae are so placed that part of the articulation is with the vertebra above and part with the vertebra below, overriding the intervertebral disk, the location of the joint being just in front of the articular process. The two lower ribs form their articulations with the sides of the vertebrae, the eleventh and twelfth, and do not override the intervertebral disks.

The costotransverse joints are usually placed with the articular surface on the anterior part of the transverse process, but at times the articulation is actually on the top of the process, with all possible variations between these two extremes. If the articulation is on the top of the process, the surface is at times horizontal, while at other times it is oblique. Sometimes the location of this transverse joint varies in the same individual, with several of the vertebrae, usually in the middle section, having their articulation on the upper part of the transverse process, while the other ribs have it directly in front (Fig. 1).

Another important feature in the function of the rib joints is the length of the transverse processes. Sometimes they are very short, at other times long, and the difference that the length of the process makes on the leverage that the main part of the rib exerts on the costovertebral joint is obvious.

The range of motion in the rib joints is limited by the anatomic structure and by the muscles and ligaments, the extreme range of motion being enough to allow movement of the thorax in full respiration to yield between 7 and 12 cm. difference in chest circumference. To ensure the normal use of these joints, the neutral position, that is, one about midway between that resulting from full inspiration and that resulting from full expiration, should be maintained, and to obtain this the ribs should slope downward from the spine about 30° (Fig. 2).

As the body is often held, the chest sags and the head and shoulders are rounded forward so that the ribs hang below the normal low point of rib function (Fig. 3). This means that the muscles and ligaments are out of balance, and that strain continued for any length of time must result in weakness and joint irritation. The position of a rib when the chest is lowered depends to a considerable extent on the position of the costotransverse joint, since if the articulation is on the

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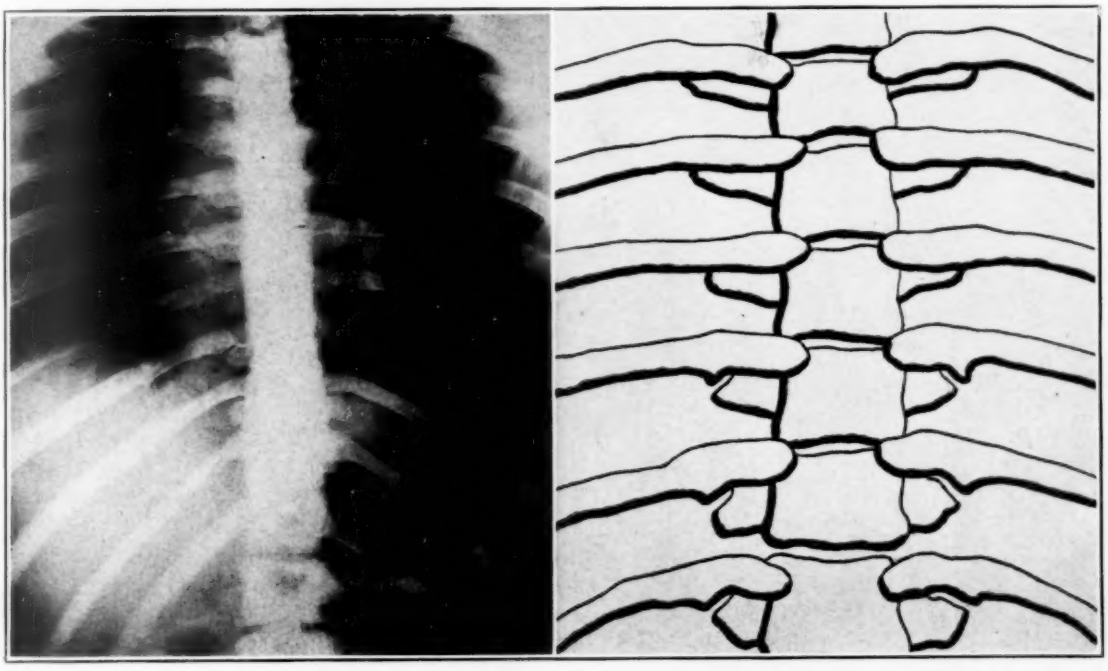
top of the transverse process, sagging of the rib must either rotate the head out of its normal position or act as a fulcrum and pry it up above that position. Regardless of whether the costotransverse articulation is on the top of the transverse process or in front, as the rib sags this joint is used as a fulcrum and the rib is either twisted, thus rotating the head abnormally, or actually forced into a different position from the normal one (Fig. 4). With the rib joints, as with all others, if these faulty positions are long maintained irritation must result, with consequent changes in structure — true arthritic conditions (Fig. 5).

In such a condition, the symptoms resulting from the mechanical strain may be referred to the region of the costovertebral joints at the back, or along the sides of the chest, owing to the fact that at the level of each costovertebral joint a nerve trunk — the intercostal nerve — leaves the spine and passes along the rib, and irritation of the root of this nerve naturally refers symptoms to its distribution. Today very few of the cases of pain referred to the back of the leg, formerly called "sciatica," are treated with reference to the leg condition, but it is realized that most cases represent referred pain from conditions in the low back. So also, many cases of pain referred to the chest wall or around the body at the different levels, with nothing apparent in the chest examination, are easily explained by irritation of the intercostal nerves at the costovertebral joints.

The circulatory disturbances often seen in connection with the irritation of these joints may be explained when one realizes that at the side of the spine, adjacent to the costovertebral joint, there is not only the root of the nerve supplying sensory and motor control, but also a ganglion of the sympathetic nervous system which is connected with the other cells of the system.

Commonly the disturbances in the rib joints are gradual in development and the symptoms are subacute or chronic. At times, as the result of definite wrench or injury, the irritation of the joint becomes much more marked and represents a true acute joint strain, with intense suffering and at times actual displacement of the head of the bone. In these cases the effect on the sympathetic ganglion is much more marked, and flushing of the face, with a change in the general superficial circulation, is likely to occur.

Once it is realized that these are true joints, subject to strain from overuse or violence exactly as with any other joint, it will be understood why they are liable to disease or injury like any other



A B

FIGURE 1.

A is a reproduction of an x-ray film showing the costotransverse joint of several of the lower ribs located on the top of the transverse process, while in the ribs above, the articulation is on the anterior part. B, a drawing made from this film, shows these joints more clearly.

joint. One of the common manifestations of disease is the atrophic type of arthritis (Fig. 5), which many times goes on to the complete ankylosis of these joints, so that no motion of the chest is made in respiration. When this stage has been reached, naturally the pain is largely overcome because there is no irritation of the joint as the result of motion.

Once this condition is recognized and the normal mechanics of the joint are understood, the

FIGURE 2.

This x-ray film shows a normal chest with the ribs in satisfactory position, the downward inclination below the horizontal being about 30°.

treatment naturally consists in having the body so held that the neutral position will be with the ribs midway between the position of full inspiration and that of full expiration. Often in order to obtain this effect, mechanical supports are needed until the joints have recovered from their irritation, or until the muscles have been so developed that the neutral, normal position is possible.

If there is extensive disease of the joints so that ankylosis becomes probable, it is also important that the ideal neutral position be obtained, since in this position the strain that must be placed on the diaphragm when the thoracic movement is eliminated will be less than would be the case if the chest markedly sagged.

Since there is no costotransverse articulation to limit the motion of the main joint, and since the rib is not supported in front by the costosternal cartilage, the floating ribs, two on each side, are able to sag and move about much more, naturally with much greater strain on the rib joint, and with much greater possibility of irritation of the nerve root and trunks (Fig. 5). The posterior position that these ribs frequently assume must mean not only a marked backward position of the rib itself, with strain to the joint, but twist of the rib as well (Fig. 6). The referred pain that would come from irritation of

FIGURE 3.

This film demonstrates an extreme sag of the chest, with marked downward inclination of the ribs. The latter are considerably below the normal low position for respiration, and to obtain this position there must be a marked unnatural strain on both the costovertebral and the costotransverse rib joints.

the nerve roots adjacent to these ribs is referred to the sides of the abdomen from the pubic bone to the crest of the ilium, and it is this irritation that undoubtedly explains the so-called "abdominal pains" mentioned by Carnett.[1]

Case Reports

Case 1. O. R., a 19-year-old boy, strong and healthy, while working hard in some agricultural occupation, had a sudden sharp pain referred to the right side, extending down to the right side of the abdomen. The suffering was intense. When the patient was lying down palpation of the abdomen was almost impossible because of the extreme sensitiveness over the right side. At the same time there was extreme sensitiveness over the joints of the eleventh and twelfth ribs on the right side. The patient's general condition was good, and the blood count showed no evidence of a rapidly developing infection. As part of the examination the patient was put in the knee-hand position, getting up on his knees and hands and thus allowing the abdomen to sag; a few deep breaths were taken to relax the tension of the abdominal wall and to make it possible for the diaphragm to work freely, as was impossible with the patient lying on his back. In a few minutes the pain was alleviated and the extreme sensitiveness over the costovertebral joints on the right side at the eleventh and twelfth ribs was entirely relieved. Palpation of the abdomen also became possible.

Comment. The case undoubtedly represents one of acute sprain, with twist or displacement of the head of the rib, with resulting spasm of all the muscles related to that region, and with the pain referred to the distribution of the eleventh and twelfth intercostal nerves. Relief was obtained by placing the patient in a position in which the rib fell forward, the correction of its twist being made by the mere sag of the body. No force was required to correct it. Recovery occurred rapidly with protection of the joints for a short time, exactly as a sprain of any other joint would be treated.

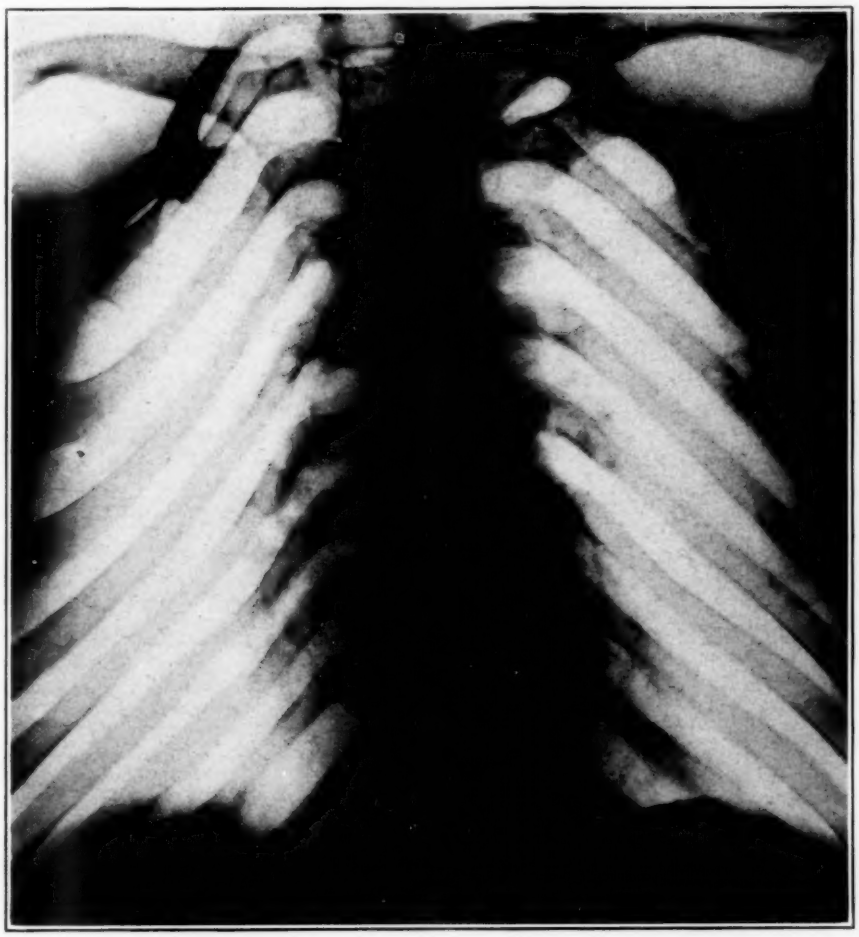


Figure 4.

This film shows not only a downward inclination of the ribs at the side but a distinct twist of the ribs so that the usual convex-upward curve is convex downward. To obtain this position the heads of the bones must be pried upward and forward.

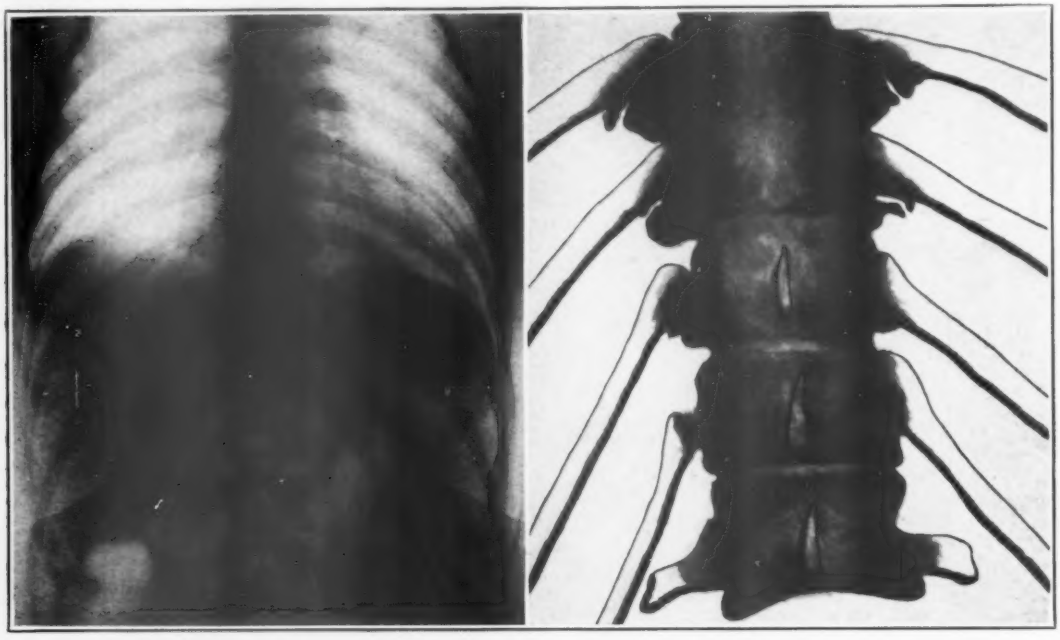
Case 2. B. L., a 45-year-old woman, had had a great deal of difficulty referred to the abdomen over a period of years, for which six different abdominal operations were performed without relief of the pain. After much treatment the actual condition of irritation of the costovertebral joints was recognized, proper treatment was given, and the abdominal symptoms were entirely relieved.

Comment. This case represents an arthritis of the costovertebral joints which had lasted for many years, with irritation of the intercostal nerves. The condition was relieved by correcting the position of the ribs and allowing the irritation at the joints to clear. Some of the pain had

been referred to the anterior part of the ribs in the region of the liver, and the difficulty had been thought to be due to gall-bladder disturbance.

Case 3. L. G., a 60-year-old woman, had been in rather poor health and was beginning to develop an arthritis involving the spine and several of the other joints. The body had been held with moderate rounding of the upper dorsal spine, and exercises were planned as a part of the treatment to correct the curve of the dorsal spine and draw the ribs up into place. After taking some of the exercises the patient had sudden, acute pain referred to the left side of the chest, covering the distribution of the fifth and sixth intercostal nerves. The pain was so intense and the suffering was so great that the case was considered to be one of angina, with probable disturbance of the blood vessels of the heart. The patient was at once removed to the hospital by ambulance. Careful study was made of the heart with all the modern, approved methods, but no evidence of cardiac disease was found. In attempting to explain the symptoms, marked sensitiveness was noted over the costovertebral joints at about the fifth and sixth vertebrae. The acute symptoms were undoubtedly due to the fact that with the exercises given to improve the function of the upper dorsal spine some of the adhesions of the rib joints had been broken, with resultant acute irritation. Recovery from the acute strain was entirely normal, and the patient has had no further attacks, nor has there been any other evidence of cardiac or vascular disturbance.

Case 4. S. M., a 33-year-old woman, was seen because of pain referred to the upper part of the chest, chiefly on the left side, and extending somewhat into the left arm. The condition had been present for some time and had limited the patient's activities. Because 2 years previously she had had a small tumor, which was said to be benign, removed from the left breast, naturally she and her physician feared that the condition was a recurrence of that disease.



A B

Figure 5.

A represents the x-ray film of a spine completely fused throughout the dorsal region from atrophic arthritis, with the rib joints also involved. The thickening about the costotransverse joint is very marked. Note also the downward inclination of the last ribs and the fact that on the right side the rib is practically in contact with the tip of the transverse process of the first lumbar vertebra, enough to cause pain from pressure on the intercostal nerve with reference along the side of the abdomen.

B, a sketch made from the film, shows the thickening about the rib joints. The complete fusion of the spine is indicated by the darkening of the whole spine, and the low position of the rib on the right side is clearly shown. The artist has made the vertebrae appear more dense than normal, while as a matter of fact the bones were much atrophied, with fusion of the intervertebral disks.

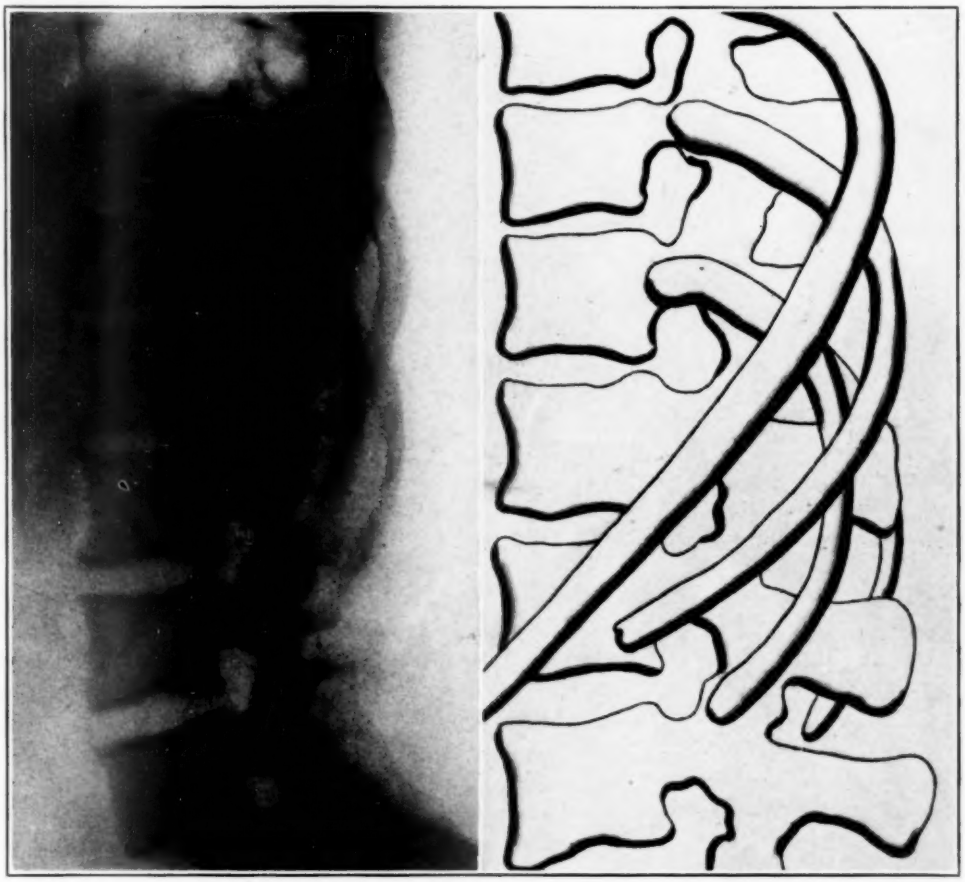
In the examination of the patient the body was held with the chest extremely low and quite flat in front, the dorsal spine rounded forward, the shoulders markedly sagged and the diaphragm naturally low. At the first examination there was marked tenderness over the costovertebral joints in the region of the fourth and fifth ribs, especially on the left side. The condition was recognized and the patient was admitted to the hospital, where the mechanical condition was overcome, with entire relief of the symptoms, a gradual lessening of the sensitiveness over the costovertebral joints and great mental relief to the patient.

These cases are used simply as suggestive or illustrative of disturbances at the different rib levels, but once one understands the rib-joint mechanism,

it becomes possible to realize that any of these forty-four joints may become irritated, strained or diseased, with the added possibility of irritation of the nerves adjacent to the joints and pain referred to the distribution of the special nerves.

Summary

There are forty-four true rib joints: twelve costovertebral joints on each side where the ribs join the spine, and ten on each side of these where the ribs touch the tips of the transverse processes at their angles. Each of these joints represents a true joint and is capable of disease or strain, as is any other joint. Since the chest is constantly used in respiration, the fixation of the rib joints in connection with disease is more difficult than it is in other joints, and the best position for rest is one with the chest held in a position halfway between the extremes of inspiration and expiration. Since there is a nerve which leaves the spine just at the level of each vertebra adjacent to the head of the rib, irritation of these nerves in connection with disease of the rib joint is easy to understand. Also, since there is a sympathetic ganglion connected with the nerve adjacent to the head of the rib, some of the circulatory disturbances undoubtedly find their explanation in irritation of this ganglion.



A B

Figure 6.

A *is a lateral x-ray film showing the downward inclination of the low ribs, with the marked posterior position commonly seen. To obtain this position the rib joint must not only be strained but the rib more or less twisted.*

B *is a drawing made from the film.*

Once the anatomic and mechanistic condition is appreciated the treatment of disease of the rib joints should be fairly simple.

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PRIMARY ECHINOCOCCAL CYST OF THE UTERUS*

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ECHINOCOCCAL disease is rare in this country, and merits particular mention when it presents itself as a primary intrinsic tumor of the uterus. To our knowledge, the following case is the only one of its kind reported from North America.

Schatz[1] in 1885 collected 14 cases from the literature. Secheyron and Pean[2] nine years later added 4 cases. In 1918 Turenne[3] and in 1920 Bull[4] each described 1 case. Nurnberger[5] in 1926 reviewed the literature and brought the count to 30, exclusive of the cases reported by Turenne and Bull. In the subsequent nine years, 9 more scattered cases were culled from the literature by Missirloglou and Anagnostidis,[6] who added 1 case of their own, bringing the total to 42. We believe that ours represents the forty-third reported case of primary echinococcal cyst of the uterus.

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CASE REPORT

A 77-year-old, Albanian-born, married woman was admitted to the Genitourinary Service of the Worcester City Hospital on August 9, 1939, because of urinary retention and lower abdominal pain of 3 days' duration.

Physical examination revealed a well-developed, poorly nourished, woman in no acute distress. The lower abdomen presented a large, firm, slightly tender, immovable tumor in the midline. The liver, spleen and kidneys were not palpably enlarged. Pelvic examination showed a small polypoid mass protruding from a marital introitus. The uterus, apparently the source of the tumor, extended 7.5 cm. above the symphysis pubis. It was firm, suggestively fluctuant and fixed. The adnexa were not remarkable.

FIGURE 1. *Echinococcal Cyst of Uterus.*

The fibrous cyst cavity in the uterus is in the center of the photograph; the mother and daughter echinococcal cysts are seen at the sides.

The urine (catheter specimen) was acid and straw-colored, with a specific gravity of 1.016. It contained a slight trace of albumin, a few red and white blood cells, and squamous cells. The red-cell count was 3,750,000, the hemoglobin 70 per cent, and the white-cell count 9000 with 84 per cent polymorphonuclears, 14 per cent lymphocytes, 1 per cent large mononuclears, 1 per cent nonsegmented cells and no eosinophils. The blood sugar was 110 mg. per 100 cc., and the nonprotein nitrogen 48 mg. Hinton and Kahn blood tests were negative.

During her hospital stay the patient's temperature vacillated between 96 and 100°F. Preparation for laparotomy was begun, but she rapidly developed symptoms of cardiac

failure and died on the ninth hospital day. At that time it was thought that she had either an adenocarcinoma or a fibroid of the uterus and that the protruding mass was a cervical polyp.

At autopsy the abdominal cavity contained no free liquid. The uterus measured 14 cm. in diameter and filled the entire pelvis. It was symmetrical and presented a smooth, pinkish-red surface. On section a cyst 13 cm. in diameter was found in the posterolateral wall. The cyst was well circumscribed by a pearl-white mantle varying from 1 to

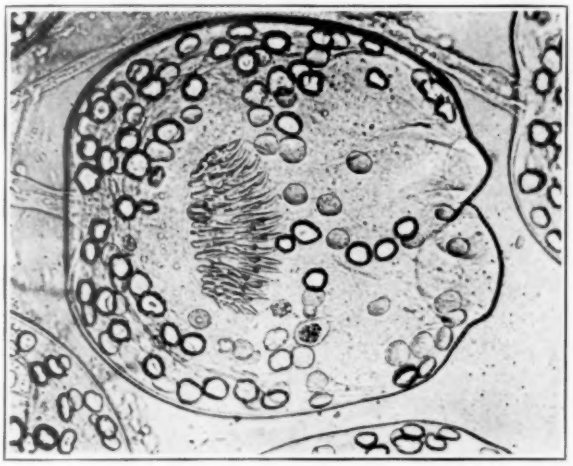

FIGURE 2. *Scolex of Echinococcus.*

This was photographed alive, unstained and nonmotile in the natural cyst fluid; the head is retracted. Note the double ring of hooklets in the center.

2 mm. in thickness. One part of its surface presented small, irregular granulations. It contained clear, whitish fluid within which a few small whitish granules about 1 mm. in diameter floated freely. Approximately a hundred smaller daughter cysts of various sizes, the largest of which measured 6 cm. in diameter, were present in the uterus (Fig. 1). These were all discrete and pearl-white, were provided with thin, translucent membranes and contained clear liquid and whitish granules similar to those in the parent cyst. No other abnormalities were encountered in the uterus, except a polyp in the cervix. The tubes and ovaries were normal and not attached to the cyst. No cysts were found in the liver, kidneys, spleen or pleural or peritoneal cavities. A small amount of purulent material was found in both ureters and kidney pelves.

A few of the granules floating inside one of the larger daughter cysts were put on a glass slide, crushed and examined microscopically within 4 hours after death. Vast numbers of scolices were seen. Most of them were discrete and almost round, with a slight flattening of the cephalic end. Orientation of the scolex depended on the direction of the two rings of hooklets which by virtue of their different refractility were clearly seen to be embedded deeply in the center of the organism. The cephalic flattening and the central nature of the hooklets were found to be results of retraction of the tip or active portion of the scolex, in which the rings of hooklets were inserted (Fig. 2). These forms of scolex were evidently early, and exhibited no movement until an addition of formalin to the medium brought forth several violent shudders, culminated by a dark discoloration of the protoplasm and a failure of response to further stimuli. Scattered through the remainder of the protoplasm were many large vacuoles, of discrete nature and not forming any pattern.

A very few other forms of scolex were present, and from their slightly larger size and continuous activity were obviously more adult than those described above. They were pear-shaped, the narrower portion of the pear being represented by the protruding head of the scolex, which remained in continuous motion and defied photography, since it swayed from side to side and alternately protruded and retracted. The double ring of hooklets was situated at the stem of the pear, or at the most actively moving portion of the scolex (Fig. 3). Almost complete retraction and reversion to the earlier quiescent form was accompanied by the introduction of a slight amount of formalin. The protoplasm coagulated and darkened, and then the violent movements ceased, the head protruding somewhat. No free hooklets were seen in any of the cyst fluid examined.

Echinococcosis of the uterus may be primary or secondary, but is usually secondary. It is often the result of a generalized peritoneal seeding,

FIGURE 3. *Scolex of Echinococcus.*

This was photographed in the motile stage, with the head protruding. The protoplasm is darkened by formalin, which was used to eliminate motility for photographic purposes. Hooklets can be seen around the neck of the organism.

particularly in the posterior cul-de-sac. Primary infection most likely occurs directly via the vaginal canal. The primary cyst is comparatively voluminous; secondary cysts are smaller and multiple. The cyst varies in shape but is generally spherical; it is smooth and firm, and insidious, without functional disturbances. The cyst is painless, and in most cases develops as a slowly expanding, space-occupying tumor compressing neighboring organs — the bladder, rectum and ureter — and resulting in slight pain in the lower abdomen, becoming severer and radiating along the lower extremities. Exploratory punctures cannot be condemned too strongly, for a variety of reasons. Skiagraphy is of decided diagnostic value for echinococcosis of the lungs, liver and kidneys,

but is practically useless when the uterus is involved, because of the pelvic shadow. Biological methods such as skin tests have been utilized to reveal the presence of echinococcal disease. As shown in cattle by Goodale and Krischner,[7] the skin test is more reliable than the complement-fixation test. The clinical outcome of echinococcosis of the genitals is the same as that when other organs are involved, namely, spontaneous cure, suppuration, discharge into some neighboring organ or death from hydatid cachexia. The first is exceptional. Primary echinococcal disease of the uterus may be first discovered at autopsy, as in this case. Secondary manifestations of pressure may be very dramatic and even cause death. If and when diagnosed, primary echinococcosis of the uterus should lend itself very favorably to surgery.

Summary and Conclusions

Forty-two cases of primary echinococcal disease of the uterus have been described in the literature. Our case is the forty-third and is, to our knowledge, the first to be reported from North America.

Its diagnosis, clinical course and treatment are briefly discussed.

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MENTAL PROBLEMS OF MID-LIFE*

A Review of 100 Cases

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During the past decade, a great deal of attention has been focused on mental illness occurring in the younger age group. Mental hygiene, with its child-guidance clinics, has devoted much effort to early attack on, and prevention of, mental disorders. During the same period, the much publicized "shock therapies" have practically monopolized the center of the psychiatric stage. More recently, as hospital statistics have shown a rapidly increasing incidence of arteriosclerotic and senile illnesses, fresh interest has been aroused relative to the mental diseases of old age. Less attention appears to have been given to the mental problems of the middle-aged group.

The designation of definite age limits for the middle-aged group constitutes in itself a controversial issue. Few people are prepared to admit that they have already strayed from the alluring paths of flamboyant youth to the more conservative highway of middle age, and fewer still will agree that they have begun to descend the hazardous pathway to old age. We may disregard the well-known adage, "Life begins at forty," and for purposes of academic discussion accept the age span of forty to sixty as representing the middle-age period.

Somewhere in this age group, the individual reluctantly awakens to the necessity of abandoning the fearless aggressiveness of earlier years, to rest, only too often, lethargically content in a false sense of self-satisfied complacency, or to permit himself to be weighed down by the depressing outlook of progressively declining physical and mental capacities.

Yet it is in this period that life places on both men and women its greatest responsibilities: maintaining the home, educating the children, meeting social obligations, ensuring economic independence and retaining physical and mental fitness, without which the fulfillment of all these responsibilities inherent to mid-life becomes exceedingly difficult. Persons belonging to this group, according to Kahn and Simmons,[1] "are taken for granted, and apparently they are not supposed to have problems." They add, "In fact they are the people who set out to solve the problems of youth and old age." As they aptly point out, settling other people's difficulties may prove a problem in itself, and may suggest a beam in one's own eye.

Just how complex and overwhelming are the problems of middle age? What are the common pitfalls of this period? These are some of the questions which we shall attempt to answer.

Consider first the responsibilities of the home: food, shelter, clothing and the maintenance of

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health, — the very essentials of existence, — not only for the individual himself, but for the marital partner, the offspring and perhaps other dependent relatives. These responsibilities form a constant source of anxiety and worry for the man or woman who has arrived at mid-life and who is expected to provide for them.

It is at this stage of life that the problem of the education of children reaches its peak. The child has matured into manhood; he has reached the college age. It is at this moment that a place must be found for him in the realm of industrial economy. Hence the necessity, often at the cost of much hardship and deprivation on the part of the parents, of procuring for the child the wherewithal to attain these ends.

If we consider the individual from the standpoint of his social obligations, we find that it is between the ages of forty and sixty that society exerts its most pressing demands. It is no longer sufficient for him simply to participate in the various social activities of the community; he is now expected, by reason of having reached the so-called "age of wisdom," to assume a place of leadership in the social field, not only for the benefit of his own age group, but also for the fostering of the social requirements of youth and old age.

Of still greater importance to the person of middle age is the responsibility of assuring economic security, which forces him to face the increasingly pressing realization that there remains only a limited time for the creation of that financial independence which he has only recently come to recognize as a necessity. This problem naturally fosters anxiety and apprehension, which may tend to be in various stages of repression. Furthermore, while he is struggling to ensure the security of his own financial position, he is often confronted with the necessity of helping others to become economically stable. There are, of course, variations in the seriousness of the situation, just as there is a wide difference in the most suitable age for different occupations. For example, the professional athlete is already on the wane in his late thirties, or even earlier, while at the same period of life the professional man — the doctor, lawyer or teacher — has just begun his career. In either case, problems result, with their major assault on the individual within the arbitrary age limits chosen in the present study.

What of the physical changes, with their mental repercussions, inherent in middle age? Biologically, it is in this group that we find the truly "dangerous age." Woman becomes the unfortunate heir to the climacteric, with its well-recognized physiologic and nervous-system maladjustments. She is beset by mild or severe depressions, irritability, fear and the knowledge of "having done those things which she ought not to have done, and of having left undone those things which she ought to have done." Man may or may not be subject to a similar physiologic and nervous upheaval, but certainly we frequently see a clinical syndrome closely simulating the female involutional changes, occurring at the stage of life corresponding to the climacterium.

There appears also, at this stage of life, the need for drastic curtailment of physical activities. Those once indulged in freely and with impunity become no longer permissible. In a vain attempt to disregard these limitations, the man of middle age may overtax himself and bring about a state of nervous exhaustion requiring hospital care. On the other hand, if he recognizes the boundaries placed on his activities by the advancing years, he may unwisely drop all physical recreation to the point of finding himself totally without physical outlet, a situation which is hardly conducive to optimal mental health.

The importance, at this crucial age, of the sex factor in the pathogenesis of mental diseases cannot be overestimated. This is particularly true of the neuroses. Phobias, many of them carried over from childhood and adolescence, others peculiar to this age, frequently result in partial or total mental disability. Hidden feelings of guilt resulting from faulty sexual hygiene, the harmful effects of which are so frequently misunderstood and exaggerated, or following sexual indiscretions in the case of physical incompatibility of the marital partners, tend to disturb profoundly the normal mental equilibrium of the individual. Gradual failure of sexual vigor, impotency and fear of impotency, and religious, social and legal barriers to the sexual outlet, following loss of the marital partner, either through death or separation — any of these problems may be operative as the source of the patient's symptoms. The etiologic importance of sex difficulty is only rarely obvious. More often than not, the underlying causal factor will be found to be masquerading under the cloak of one or more of a multitude of clinical manifestations, such as alcoholism, restlessness, agitation, hysteria, neurasthenia, apathy, depression, perhaps leading to self-destruction, excessive erotism, sexual promiscuity and many others. The semeiologic polymorphism characteristic of the sexual problems of these years precludes any attempt at numerical evaluation in as limited a study as the present one.

We have mentioned only some of the problems of the middle-aged group which, when improperly handled, become precipitating factors in the development of nervous and mental reactions that are frequently severe enough to require hospitalization.

It is a well-known fact that most admissions to public institutions treating mental diseases do not fall within the forty-year to sixty-year age limits. On review of the admissions to the Ring Sanatorium and Hospital during 1937, 1938 and 1939, however, we have been interested to find that of a total of 849 patients, 356 (41.9 per cent) were in this group, even though the ages of those admitted ranged from eighteen to ninety-six. In other words, nearly half the total admissions were in the middle-aged group. However, most of those who came to the sanatorium for the treatment of alcoholism and drug addiction also proved to be within the ages of forty to sixty. These figures, as we have said, include all admissions, but the necessity for fixing some boundaries has caused us to limit the cases to 100 having definite mental symptoms, and occurring in the delineated age group.

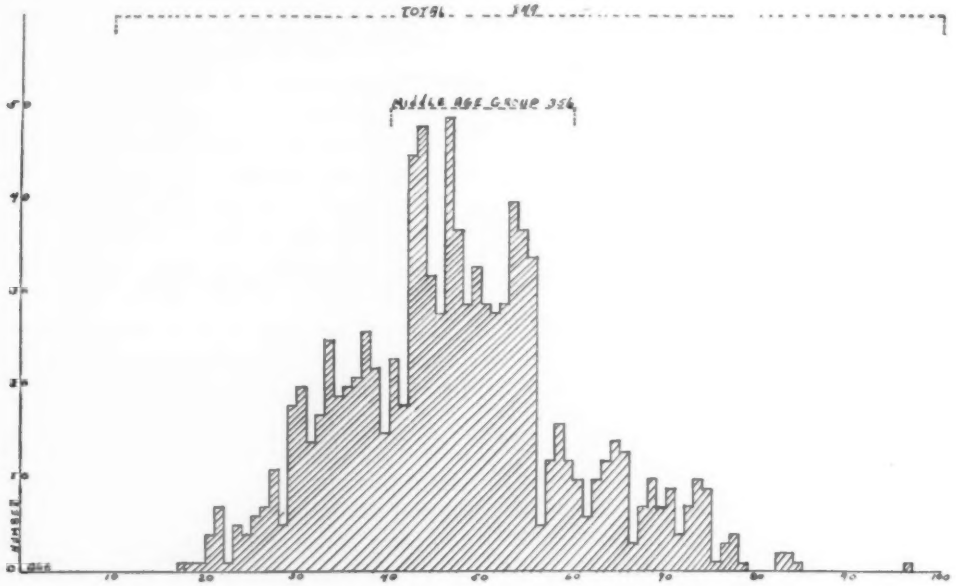

FIGURE 1. *Graph Showing the Admissions for 1937, 1938 and 1939 in Relation to Age.*

What is the reason for the higher admission rate in the middle-aged group, as compared to that reported from public institutions? We offer a two-fold explanation: in view of the unfortunate general attitude toward mental illness, every effort must be directed, at this particular period, toward the protection of the individual from any so-called "stigma"; secondly, it is at this wage-earning period that people are best able to afford this protection. The same reasoning appears to hold good in the drug and alcoholic group. In a sense, a majority of these persons might well be included among those classed as having mental illness, as neurotic and psychopathic symptoms are in great prominence. We have excluded, however, all cases of drug and alcohol addiction without mental symptoms, in order to make the picture clearer and to keep it within well-defined limits.

Among this group of 100 cases, 72 fell within the so-called "functional group"; that is, they failed to reveal any evidence of organic change in the nervous system associated with mental symptoms (Table 1). Twenty-four of these were classified in the manic-depressive group, with 18 in the depressive phase. Involutional melancholia was the accepted diagnosis in 18 of the 72 cases. To the latter classification we have admitted only those patients having symptoms of depression, agitation and self-accusatory ideas customarily associated with the involutional state. We have not included those having a history of previous attack. The psychoneuroses were next in frequency, with a total of 16 cases. Most of these patients had had previous episodes, but the stress of mid-life had again precipitated symptoms requiring institutional care. Schizophrenia was represented by only 6 cases. This is not surprising, since schizophrenia is essentially a disorder of youth. Four cases were labeled psychopathic personality, and 4, paranoid condition.

Among the organic group, 17 cases were represented, the most frequent condition being psychosis

with cerebral arteriosclerosis, which appeared 7 times. General paresis or syphilitic meningoencephalitis accounted for 4 cases, traumatic psychosis for 2, and Pick's disease, taboparesis, postencephalitic syndrome, and psychosis with other somatic disease for 1 each.

The remaining 11 cases were divided among the following diagnoses: 2 each of toxic psychosis,

TABLE 1. *Classification of Psychoses.*

DIAGNOSIS		NO. OF CASES	
Functional psychosis			72
Manic-depressive psychosis		24	
Depressed	18		
Manic	6		
Involutional melancholia		18	
Psychoneurosis		16	
Schizophrenia		6	
Psychopathic personality		4	
Paranoid condition		4	
Organic psychosis			17
Cerebral arteriosclerosis		7	
General paresis		4	
Trauma		2	
Pick's disease		1	
Taboparesis		1	
Postencephalitis		1	
Psychosis with other somatic disease		1	
Toxic psychosis			9
Toxic psychosis		2	
Drugs		2	
Delirium tremens		2	
Alcoholic hallucinosis		2	
Korsakoff's psychosis		1	
Undiagnosed psychosis			2
Total			100

psychosis with drug addiction, delirium tremens, alcoholic hallucinosis and undiagnosed psychosis, and 1 case of Korsakoff's psychosis.

In consideration of the etiologic factors which we have reviewed, we should expect to find depression and its associated phenomena, weeping, self-condemnation and somatic complaints, occupying the most prominent place among the symptoms. This proved to be true, with an incidence of 39 cases (Table 2). The next group of symptoms in point of frequency were those in the sphere of agitation, restlessness, irritability and insomnia, which occurred 22 times. Anxiety, worry, apprehension, nervousness and preoccupation also occupied a prominent place, and were given as the initial symptom in 16 cases. Other symptoms were: disturbances of sensorium, such as confusion, failing memory and irrational state, 8 cases; physical symptoms, weakness, headache, parotitis, hemiplegia and tremulousness, 5 cases; obsessions, compulsions and phobias, 5 cases; hallucinations, 2 cases; and exhibitionism, dysphagia and drowsiness, 1 case each. In 7 cases the symptoms were so indefinite that they are of necessity classified in more than one group.

The average hospital residence of the 100 patients was 47 days. A review of their condition on discharge reveals that 13 were regarded as recovered, 54 as greatly improved, and 32 as unimproved; 1 was deceased.

It is interesting to note that suicidal threats were made by 24 patients, and that 6 of these made suicidal attempts, either before or during hospitalization. One successful attempt was made by a patient who had left the hospital without permission. The presence of a history of mental illness in the family antecedents of 20 of these 24 patients, and of a suicidal history in the antecedents of 5, reveals an important hereditary influence.

One cannot stress too much the importance of removing the patient to the friendly atmosphere of a hospital, where close nursing and medical supervision are available at all times. We have shown the preponderance of the depressive states during the mid-life period. Proper supervision of a suicidal patient can best be secured in a hospital where specially trained nurses know the value of constant vigilance.

In the way of therapy, the accepted methods were employed. Special care was given to the

TABLE 2. *Initial Presenting Symptoms.*

SYMPTOMS	NO. OF CASES
Depression	39
Weeping, depression	
Self-condemnation	
Somatic complaints	
Hypoactivity	
"Blue spells"	
Agitation	22
Restlessness	
Agitation	
Irritability	
Insomnia	
Anxiety	16
Worry	
Preoccupation	
Apprehension	
Nervousness	
Confusion	8
Failing memory	
Confusion	
Irrationalism	
Personality change	7
Mood swings	
Paranoid ideas	
Grandiose ideas	
Obsessions	5
Phobias	
Compulsions	
Physical symptoms	
Weakness	
Headache	
Hemiplegia	
Tremulousness	
Parotitis	
Hallucinations	2
Exhibitionism	1
Dysphagia	1
Drowsiness	1
Total	107

physical condition of the patient, and every effort was made to treat and correct any organic disease. Hydrotherapy was used in those cases in which the patient was disturbed, tense, anxious, depressed or excited. We have used the neutral tub bath,

the continuous-flow bath, the cold and neutral wet-sheet pack and the various sprays and douches. The psychotherapy employed was of the suggestive and re-educational types. Occupational therapy, both formal and in the patients' rooms, and outdoor exercise formed important features of the daily schedule. Electrotherapy appeared to be of value, particularly in certain organic conditions, and in some of the psychoneuroses. Special therapy was resorted to for the organic manifestations of general paresis and for the treatment of menopausal symptoms. In general paresis, malarial and artificial fever therapies were used, in conjunction with chemotherapy; while in the menopausal deficiencies, replacement hormonal therapy gave good results. Shock therapy (Metrazol and insulin) was not used in any of the cases of schizophrenia represented in this group, since none were suitable for such treatment.

We present in brief form the essential features of 3 cases regarded as typical of the predominant group: 1 of psychoneurosis, 1 of involutional melancholia, and 1 of manic-depressive psychosis (depressed).

Case Reports

Case 1. M. I. M. (No. 4771), a 44-year-old, married woman, was admitted on December 31, 1938, and was discharged on February 18, 1939. There were irritability, loss of strength and many somatic complaints. The family history was negative. The patient's mother died when she was 3½ years of age, and she was brought up by her grandmother. She had had the usual childhood diseases. She had had an appendectomy and a tonsillectomy and adenoidectomy as a child, influenza followed by bilateral lobar pneumonia in 1919 and a right salpingo-oöphorectomy in 1937. During adolescence she suffered a fracture of the right arm and of the right second toe. She completed high school and attended a teachers' college for a short period, then studied voice. She was a concert singer in this country and abroad for 15 years. She was married at 28. At first her married life was happy; she then found that her husband was unfaithful and that he was an alcoholic addict. There had been no pregnancies. The patient was described as high-strung, very sensitive and introspective. Her habits were good, except for the use of barbiturates for a number of years.

In 1929, during the financial depression, she became worried, unhappy and run down. She had periods of fainting, then alternating periods of feeling well and feeling ill. Since that time, on three occasions, she had spent periods of 2 to 5 weeks in hospitals. In the 3 years before her admission, her husband had been very neglectful and frequently humiliated her. She described strong feelings of insecurity and shame, and a tendency to shun other people and feel sorry for herself, and stated that she had had friction with her husband's relatives. She felt weak, exhausted and irritable, and complained of pain in various parts of her body.

At physical examination the patient was undernourished. There was definite tenderness over both antrums. The pupils were unequal, the right being greater than the left. The upper jaw was edentulous, and there were several teeth missing from the lower jaw. There was a pleural friction rub over the right chest. The blood pressure was 164/100, dropping to 144/90. There were old healed operative scars on the abdomen, and there was a slight scoliosis to the right. A blood Wassermann test, x-ray examination of the chest, an agglutination test for undulant fever and a urinalysis were negative. There was a mild secondary anemia.

Mentally the patient was, for the most part, pleasant, but at times she was unstable. There were many hypochondrial complaints, such as dyspnea, anxiety and a sensation of tightness in the back of the neck. On one occasion she slumped to the floor, following which there were no abnormal findings.

The patient discussed her family problems freely. She expressed feelings of insecurity and a desire to do something for herself, yet she could not decide to extricate herself from the home situation. During the first part of her residence she ran a low-grade fever, which cleared later. She was treated by psychotherapy, sedation, hydrotherapy and electrotherapy, massage and occupational therapy. She improved slowly during her stay in the hospital, and at the time of discharge was greatly improved.

Case 2. G. B. (No. 4869), a 46-year-old housewife, was admitted on October 4, 1939, and discharged on November 10. She was readmitted on January 7, 1940, and discharged on February 3. The family history was essentially negative. The patient's infancy and childhood were not remarkable. She graduated from high school and attended business college. Immediately following graduation she married a salesman. Her marital life was very happy. There was one daughter about to be married; this the patient resented. The menses had begun at 14, and there had been no abnormality until 1928, at the age of 34, when they became irregular and scanty. Three years later she developed menorrhagia (10 days to 2 weeks). She had continued to be troubled with menstrual dysfunction until the present time. Her last period prior to the first admission continued for 17 days. She was described as cheerful, friendly, sociable and a good mixer. She was interested in sports, her home and social activities.

The present illness began on October 13, 1938. While shopping the patient suddenly responded to an impulse to walk away with a small article from the counter, in the act of which she was discovered. Although she was fully cleared following investigation, she continued to worry and to be self-critical, and said that she was powerless to overcome the shame that she had brought on herself and her family. She gradually became more depressed, restless and agitated, and hospital care was advised. In March, 1939, she was sent to a state hospital, where she remained for 2½ months. There she was depressed and irritable, was considered suicidal and expressed self-accusatory ideas. The sensorium was clear. The patient responded well to injections of follicular hormone; at the time of discharge she was considered much improved. A diagnosis of involutional psychosis was made. On returning home she continued the use of the hormone for but a short time. Toward the latter part of the summer of 1939 all her mental symptoms returned and she was admitted to the sanatorium in October.

Physical examination was essentially negative, as were laboratory studies, including a blood Hinton test. Mentally the patient was depressed, retarded, self-accusatory and at times agitated. She talked a great deal of the shame she had brought on the family through the shopping incident. She was again given large doses of follicular hormone, and rapidly improved. Her husband

insisted on premature removal on November 10. She was readmitted in January, 1940, for further treatment. During this residence she continued to be depressed, was irritable and did not respond as before to hormone therapy. She was finally discharged in February against advice, still depressed and self-accusatory. This case is quite typical, and shows the type of severe reaction seen in women at the climacterium.

Case 3. J. H. B. (No. 4805), a 43-year-old married man, was admitted on April 20, 1939, and discharged on May 9, 1939. The family history was essentially negative. The patient's infancy and childhood were not remarkable. After graduation from high school he went to war, and on returning went into the leather business which his father had established. During the 2 years previous to admission he had recognized signs of insecurity in his position, which he had tried to overcome by attending law school at night. In December, 1938, the firm went bankrupt and he was thrown out of work. He tried various occupations, but was never able to get permanently placed. For 2 months he seemed able to adjust himself fairly well to the situation, but then became increasingly depressed. His first complaint was insomnia, then "shaking spells," and finally he became very tense and anxious. He felt guilty because he had accepted help from his father, and became self-critical, agitated, more depressed and retarded. Three weeks before admission he developed a fear that he had syphilis, then feared that his family had it, and finally was sure that everyone in town was infected with it. He was sure that his face was changing, and he would look at himself in the mirror for long periods. Hospital care was advised.

Physical examination revealed a depressed and agitated man, with a blood pressure of 200/130. There was no evident peripheral arteriosclerosis. Blood Hinton and spinal-fluid Wassermann tests and urinalyses were negative. Mentally the patient was agitated and depressed, was self-accusatory and expressed ideas of unworthiness. He retained his obsessions regarding syphilis, and was retarded in speech and thought. Three days after admission he made a suicidal attempt by diving against a radiator. He responded well to hydrotherapy, and gradually the severity of his symptoms lessened. By May 22, about a month after admission, he expressed serious doubts as to the validity of his obsessions, seemed more cheerful, was more spontaneous and admitted freely that he had made the suicidal attempt. He continued to improve, and on May 29 was discharged with a diagnosis of manic-depressive psychosis (depressed), condition improved. This picture is very similar to that seen in women in the climacteric period, and is quite typical of those symptoms in men in mid-life who have undergone serious threats to their security.

These cases are presented as typical of the more severe reactions in mid-life. Many of these are comparatively mild, but they have the potentialities of becoming acute.

Summary

The mental problems of the middle-aged group are reviewed.

A brief study is presented of 100 such patients between the ages of forty and sixty.

Three case abstracts representing the severe reactions that may be manifested in response to problems in this age period are given.

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REPORT ON MEDICAL PROGRESS

THORACIC SURGERY

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Pulmonary Tuberculosis

A CONCISE and useful treatise on pulmonary tuberculosis has been published by the Oxford University Press[1] under the joint authorship of an internist, a pathologist and a surgeon. In reviewing this book for the *American Review of Tuberculosis,* Max Pinner[2] refers to it as "the most usable book on this subject in the English language," and remarks that "the practitioner wishing to find up-to-date information will find it here in concise and digestible form." As Pinner is not given to the use of superlatives without due cause, his favorable criticism may be taken at its face value. The chapters on the pathology of tuberculosis by Pagel are particularly well done and provide an essential background for the clinical management of the disease. This aspect of tuberculosis has on the whole received scant attention in America, mainly owing to the fact that large public institutions housing tuberculous patients have in the past been poorly equipped with personnel and facilities for postmortem studies.

The chapters on the application of surgical measures to pulmonary tuberculosis are highly colored with the dictums of the Sauerbruch school, and many details are at variance with the practice of American surgeons. The recent edition of Alexander's *The Collapse Therapy of Pulmonary Tuberculosis*[3] is the authoritative treatise on this phase of treatment. A new volume, *Artificial*

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Pneumothorax,[4] has recently been issued by the Saranac Lake group, and promises to be a useful and practical reference for physicians interested in this subject.

Collapse therapy is fortunately no longer on trial, but public institutions are from time to time obliged to show justification for the additional expense necessary to maintain an adequate surgical program. A report from the Municipal Tuberculosis Sanitarium of the City of Chicago[5] records an experience with 7341 patients observed over a six-and-a-half-year period. Three thousand and ninety patients were subjected to collapse for more than three months and 337 for less than three months. In 330 cases artificial pneumothorax was attempted; 3584 patients served as controls. Broadly speaking, the results were twice as good with the treated patients as with the controls, and better still as against the life expectancy of patients with open tuberculosis as revealed in the literature. Collapse is viewed as a treatment sequence, with an ideal indication and an optimum moment for each operation.

This conception of collapse therapy as a treatment sequence is of course extremely significant. It has been expressed by metaphor as a game of chess in which a series of moves is carried out, all directed toward the same purpose. At the present time the move that is most frequently delayed is the shift from a partially successful artificial pneumothorax to a more effective collapse measure. The dangers of continuing an incomplete pneumothorax that has not converted the patient's sputum from positive to negative have been stressed for years, but the surgeon still receives a steady flow of cases of tuberculous empyema that result from such injudicious tactics.

An understanding of the pathology of the disease will also inform the operator regarding the hazards of artificial pneumothorax when it is induced early in the course of a pneumonic type of lesion or in the initial phase of benign hematogenous spread. Tubercles directly beneath the visceral pleura lead to pleural extension and the grave complication of a tuberculous empyema. The patient then becomes the victim of the treatment of the disease rather than of the disease itself.

After an initial experimental phase, the procedure of extrapleural pneumothorax is finding a very limited place in the armamentarium of the phthisiotherapist. It is not a reversible method of collapse, as is intrapleural pneumothorax, and no case is on record where an elective re-expansion of diseased lung has taken place after the lesion has become quiescent. Many operators eventually fill the space with oil and continue the collapse indefinitely. Under these circumstances thoracoplasty must be considered preferable as a primary procedure. Extrapleural pneumothorax is finding its place as a palliative measure or as preliminary to thoracoplasty. With adequate medical therapy it will rarely be needed in the latter capacity. Many reports[6–13] on the procedure have appeared in the recent literature.

The goal in the therapy of pulmonary tuberculosis is the conversion of a positive sputum to one that is free of the tubercle bacillus. This requires the obliteration of cavities; and collapse therapy, either with artificial pneumothorax or by surgical measures, is largely concerned with the closure of cavities. As the cavity has become a center of interest in the treatment of the disease, it is not surprising to find that knowledge concerning it has increased and certain new concepts have been developed. In fact, the new science of "speleology" (from the Greek σπηλαῖον, meaning "cave" or "cavern") has emerged.

The natural healing processes that from time to time bring about the spontaneous obliteration and healing of tuberculous cavities have been described at length by pathologists. Spontaneous healing is, however, such a rare occurrence that, given a demonstrable excavation, no time is lost in applying the active measures of collapse therapy if other indications permit.

It was formerly thought that the spherical shape of a cavity in the lung was a resultant of forces inherent in the elastic tissue of lung substance. It was known that cavities might be larger than the original liquefied caseous areas, and the mechanism involved was pictured by placing a sheet of rubber under tension and piercing it with a pin. The size of the resulting hole depended on the degree of tension to which the rubber was subjected. In certain texts a cavity in the lung was shown in the form of a diagram in which the circular defect was surrounded by small spiral springs arranged radially about the circumference.

In 1930 Pearson[14] demonstrated a high positive pressure within air-containing cavities, an observation that has led to quite a different concept of the mechanical forces involved, and has suggested certain new therapeutic procedures.

Coryllos[15] extended observations on the pressures within air-containing cavities and also inspected their interiors with a small thoracoscope. He attributed the positive pressure to partial bronchial occlusion that acted as a one-way valve. Air under tension entered the cavity in the act of coughing and was trapped so that it could not escape. If the bronchial occlusion became complete, the first manifestation was the appearance of a fluid

level; then, as the air was absorbed by the blood stream, the cavity became smaller, even to complete disappearance. These observations furnished a reasonable explanation for certain puzzling phenomena that had been observed from time to time by many clinicians. Large cavities with thin walls had been observed to appear within a short space of time and to vanish completely in the same abrupt and unexplainable manner. In other cases cavities remained unaltered in size by a complete artificial pneumothorax. Eloesser[16] presented a detailed description of the behavior of "blocked" or ballooned cavities in his presidential address before the American Association for Thoracic Surgery.

It was suggested[17, 18] that all would be well if a bronchus could be permanently occluded by artificial measures, and experiments with animals were initiated to find a method that could be applied clinically. About this time, however, both internists and surgeons dealing with pulmonary disease developed a wholesome respect for the effects of bronchial occlusion as a spontaneous manifestation of disease processes.[19, 20] At the present time it is doubtful that anyone would have the temerity deliberately to produce bronchial occlusion in a patient.

A bold and ingenious step has been proposed by Monaldi[21] for dealing with this type of tuberculous cavitation through a peripheral approach. A catheter is inserted by means of a trocar directly through the chest wall into the lumen of the cavity. Low-pressure suction is applied intermittently. It is reported that cavities so treated immediately decreased in size and became obliterated within four months. Information regarding the Monaldi procedure is based almost entirely on word-of-mouth transmission at the present writing, as well-documented case reports have not yet appeared in the literature. It is, however, a logical outgrowth of changing conceptions regarding the physiopathology of cavitation.

Surgeons are beginning to consider actual extirpation of the lung in selected cases of pulmonary tuberculosis. Of course some of the earliest attempts at lung resection for tuberculosis were carried out between the years 1881 and 1895. These are recounted in treatises by Ruggi[22] and by Tuffier.[23] The subject was then dropped, and the highly successful development of collapse therapy removed the stimulus to revive what was obviously a hazardous and difficult undertaking. Two things have now happened: first, resection of the lung for other diseases has brought technical improvement and familiarity with the operation; secondly, the failure of collapse therapy in certain phases of pulmonary tuberculosis can be predicated.

In 1934, Freedlander[24] reopened the question in an address to the American Association for Thoracic Surgery, and several discussers added cases from their own experience. These cases as a rule were ones in which resection was undertaken for what was supposed to be bronchiectasis but what subsequent microscopy identified as tuberculosis. It soon became apparent that the patients did not die of generalized tuberculosis, nor did their incisions fail to heal or bronchial fistulas persist. At the present time, therefore, pulmonary resection is seriously considered and not infrequently undertaken in known tuberculous pulmonary infection when there is a serious degree of bronchial stenosis that precludes success with collapse therapy. It has also been performed for large areas of caseation and liquefaction that have not found a bronchial outlet, and is proposed for cavities so situated that the likelihood of being able to collapse them by chest-wall surgery is slight. The latter indication may well be a pitfall for the enthusiast, and should be entertained only by a surgeon thoroughly familiar with modern methods of collapse therapy.

Primary Carcinoma of the Lung

Reasons for the recent increase in the incidence of bronchial carcinoma were discussed by Boyd[25] in the 1938 Mütter Lecture of the College of Physicians of Philadelphia. During the ten-year period ending in 1936, at the Department of Pathology of the University of Toronto, the third most frequent site of primary cancer was the lung. It was exceeded in frequency only by the stomach and large bowel. The actual incidence was 1.2 per cent in 4500 autopsies. In Winnipeg the incidence was 2.6 per cent in 2408 autopsies.

The increased incidence of primary carcinoma of the lung has been a world-wide phenomenon. Explanations have been sought on the supposition of the inhalation of a carcinogenic agent. The tarring of roads and the dissemination of automobile exhaust gases are commonly cited. Boyd points out that in Winnipeg tarred roads are remarkable for their absence and that in Russia there are practically no tarred roads and few automobiles; also that in Beirut, Syria, carcinoma of the lung is as common as it is in Philadelphia, yet the patients live as did their forefathers in the days of the Pharaohs. He defends the thesis that knowledge of the disease has spread over the world and is the most important element in the apparent increased incidence, and quotes MacCallum as follows regarding syphilitic aortitis: "Since

then everyone has recognized it at a glance. It seems to be one of those simple triumphs of observation that makes one ashamed of being so blind."

According to Boyd, there is no form of tumor more easily overlooked, especially if the case does not come to autopsy. The clinical diagnosis is difficult because the disease may be so long latent or occult, and because metastases frequently dominate the picture. The radiologist has learned to observe not the tumor itself but its effects in the thorax. It is more difficult to explain the fact that the leading pathologists of the nineteenth century failed to recognize it, if it really was common in those days.

The failure of pathologists to recognize primary cancer of the lung Boyd attributes to ignorance of the nature of the gross lesion, of the microscopic picture and the natural history of the disease, that is, the methods of spread and the sites of metastases. Numerous mistakes of his own department are cited. He concludes, "What we know, we see." This has been true of coronary thrombosis and is true of bronchial carcinoma. It is true for the clinician, the bronchoscopist, the radiologist and the pathologist.

Boyd's analysis is comforting to those of us who drive automobiles over tarred roads and light cigarettes at the traffic lights, because experiments with mice show that the exposure to carcinogenic agents does produce an increased incidence of pulmonary tumors. According to Campbell,[26] inhalation experiments prove that cigarette smoke gives a high incidence of lung tumors in mice as compared with controls. Soot from automobile exhausts suspended in the atmosphere gives a slight increase in the incidence, and dust from tarred roads appears to be a significant and dangerous source of carcinogenic agents.

Elaborate consideration of the statistical evidence purporting to show an actual increase in the incidence of primary pulmonary cancer may be found in a monograph compiled by Simons.[27]

A few years ago Pancoast[28] described a symptom complex produced by a malignant tumor invading the extreme apex of the thoracic cavity, or, as he called it, the superior pulmonary sulcus. A tumor in this region, he said, produces pain referred to the shoulder, arm and hand, associated with partial paralysis due to invasion of the lower cords of the brachial plexus; paralysis of the cervical sympathetic nerves, manifested by Horner's syndrome*; and evidence by x-ray of destruction of the upper ribs or vertebrae. Pancoast postulated a specific tumor arising from an epithelial (branchial) rest as the cause of the syndrome. It is now apparent that the symptom complex described by him is not a specific one, as it may be produced by a variety of tumors of different origins. The symptom complex is not an uncommon manifestation of primary carcinoma of the lung, and most of the cases encountered clinically are of this nature.

A matter of definition in regard to terminology is raised by Morris and Harken.[30] It is pointed out that Pancoast postulated a "lack of origin from lung, pleura, ribs or mediastinum." A Pancoast tumor is therefore not to be confused with the superior-pulmonary-sulcus syndrome that it produces and that is admittedly nonspecific. If it can be definitely established that a squamous-cell epithelioma arises from a cell rest in this region and produces the symptom complex described, the Pancoast eponym may be perpetuated, but it must be confined to this specific entity. Tumors of pulmonary or other origin should not be termed "Pancoast tumors" even though the superior-pulmonary-sulcus syndrome is produced. Morris and Harken believe that they can identify three true Pancoast tumors among 8 cases of apical chest tumor.

The number of cases of carcinoma of the lung that can be salvaged by surgery remains discouragingly low. Tudor Edwards[31] reports 172 cases of bronchogenic carcinoma that came under observation in two and a half years. Of these but 28 were submitted to thoracotomy as possibly operable. In 13, dissection pneumonectomy was carried out. Six patients survived after operation from six months to two and a half years. These results very closely approximate the unpublished figures of the Massachusetts General Hospital, and are of value in giving a broad view of this grim disease. Benign bronchial adenoma is still being confused with primary bronchogenic carcinoma, particularly in regard to reporting the results of surgical treatment. As I[32] have stated elsewhere:

> During the ten-year period ending April 1, 1940, a clinical diagnosis of primary tumor of the lung was made in 380 cases at the Massachusetts General Hospital. It was confirmed by microscopic examination in 172 cases, of which 155 are classified as primary bronchogenic carcinoma, 15 as adenomas or carcinoids, 1 as neurofibroma and 1 as hamartoma. The frequency of benign tumors in the entire group is but 4.4 per cent, a relatively insignificant number. The frequency calculated for the group with microscopic confirmation of the diagnosis rises to 10 per cent. If attention is directed to the group in which resection was carried out, it is found that benign lesions account for approximately 30 per cent of resectable bronchogenic tumors. If consideration is still further limited to patients surviving resection with apparent arrest of the disease, benign

*Priority rights regarding this eponym are under discussion at present. It has been suggested that the term "Hare's syndrome" should be substituted (Fulton[29] and Morris and Harken[30]).

lesions comprise 64 per cent. These figures are cited to show how important it is for surgeons and pathologists to agree in their definitions before comparing results in the treatment of pulmonary neoplasms.

Improvement in the treatment of carcinoma depends on early diagnosis. Hochberg and Lederer[33] have studied the early manifestations of primary carcinoma of the lung. In 21.6 per cent of cases, the first symptoms that brought the patient to the physician did not suggest intrathoracic new growth. In 10 of 18 cases in which the diagnosis was not established until one to six months had elapsed after first medical advice, the correct diagnosis would have been made if the physician had thought of the fact that infradiaphragmatic symptoms may be due to supradiaphragmatic disease, or if in suspicious cases bronchoscopic examination had been suggested.

In the earliest important monograph on primary malignant growths of the lung, published in 1912, Adler,[34] wrote:

> As at the present the conscientious physician examines every chest for possible tuberculosis, so in the future every chest will have to be examined for possible tumor. The writer would go still farther. Where all the means of diagnosis outlined in this little study fail, where there is suspicion of tumor, but no assurance is possible, there should be — it is emphatically here stated — as little hesitation in resorting to an exploratory thoracotomy as there is nowadays in submitting to an exploratory laparotomy.

Cysts of the Lung

An extensive literature on cystic disease of the lung has accumulated. The terminology is still confused, and a basic difficulty is encountered in differentiating cysts that are true embryologic malformations from those that are the end product of infection. Multiple cysts merge with what may be termed cystic bronchiectasis. Blebs that develop in emphysema may also be confused with other types of cysts.

Sante[35] provides an excellent bibliography of the subject, and the following suggestions as to terminology agree in part with his classification.

Congenital cyst: a cyst in which there is absolute proof of a congenital origin of the lesion or an unmistakable anomaly of architecture can be demonstrated.

Cyst: a term limited to collections of fluid formed by partial or complete occlusion of secretory glandular structure. Bronchogenic cysts may be intrapulmonary or mediastinal.

Pneumatocele: an air-filled cavity. A cyst becomes a pneumatocele with evacuation of its contents.

Bulla: an air-containing bleb arising as a result of emphysema.

Cystic bronchiectasis: a borderline entity between multiple-cyst formation and saccular bronchiectasis, combining certain characteristic features of both. Reisner and Tchertkoff[36] believe that this is a well-defined entity and conjecture a congenital origin. Attention is called to a disproportion between the paucity of subjective symptoms and extensive pulmonary changes. This condition appears similar to the *Waben-lunge* of the German and the "honey-comb" lung described by English pathologists.

Sequestration pneumatocele. Necrotizing infections may leave a large air-filled defect as a legacy. After the infection has burned out, the term "chronic lung abscess" hardly seems applicable. There may be no symptoms, or only an occasional hemoptysis. With the episode of acute infection buried in the childhood history, these may by error be assigned a congenital origin. The original infection is usually a putrid lung abscess or rarely a Friedländer-bacillus pneumonia.

Saccular bronchiectasis. When bronchial stenosis is present the obstructed bronchi may dilate to form large cysts. At times episodes of infection may break down their walls so that intercommunications exist. This condition is usually associated with a very foul sputum due to putrefaction of the retained secretions. If free bronchial drainage becomes re-established the symptoms may be relieved, leading to a classification as cystic bronchiectasis, or the postulation of a congenital origin.

A pneumatocele originating either from a congenital cyst or as the end result of sequestration may contain air under pressure. If it is large, — some pneumatoceles occupy the entire hemithorax, — the suffocative symptoms of a pressure pneumothorax may be produced. Kaltreider and Fray[37] have studied the pathologic physiology of pulmonary cysts and emphysematous bullae.

Wounds of the Lung and Pleura

It is of timely interest to refer to the subject of chest injuries as one of the most pressing problems of military surgery. Practically nothing can be learned of what is going on in the present European war, except that it may be inferred that the rapidly moving battle fronts have necessitated far-reaching changes in all methods of handling the wounded. In reviewing the experiences of the World War of 1914-1918 basic principles referable to the management of chest wounds are apparent.

In 1918, Lieutenant-Colonel Lincoln Davis and Major Frederick C. Irving were stationed at Limbraga, Italy, as near neighbors of Ospedaletto 79,

attached to the 11th Corps of the Italian Army during final action on the Piave. Directing this hospital was Major Eugenio Morelli, a pupil of Professor Carlo Forlanini, the originator of artificial-pneumothorax therapy. Morelli had given careful thought to the problems presented by wounds of the chest, and had as a particular contribution proposed the induction of artificial pneumothorax to control hemorrhage from the wounded lung. If hemothorax was present, the blood was aspirated and replaced with air. These propositions, according to Forlanini, had been formulated by Morelli several years before the war, and in fact published in 1910 in a thesis for *Libera Docenza*.[38] Davis and Irving[39] were so impressed by the methods they observed in actual use by Morelli that they found time to translate his monograph from the Italian. I have had a long acquaintance with this book as it first aroused my interest in thoracic surgery. It is highly recommended to anyone who desires to obtain a more detailed account of the subject.

The immediate mortality in chest wounds from high-explosive missiles is very great. Sauerbruch[40] examined the dead on the battlefield and found that approximately 33 per cent had succumbed to chest injuries. Duval[41] said that the mortality at dressing stations was very nearly 30 per cent, in ambulances 25 per cent and at army hospitals 15 per cent. Grégoire and Courcoux[42] gave the mortality as 25 per cent at dressing stations, 20 per cent in ambulances and 2 per cent at hospitals. Duponchel[43] reported a 30 per cent mortality at dressing stations and a 34 per cent one in ambulances. Any attempt to reduce the mortality rate of this type of chest wound must therefore be made as near the front line as possible. The matter is made more difficult by the fact that the mortality rate of non-penetrating wounds of the chest wall and penetrating wounds by bullets is low; these should be handled by conservative measures. Accurate appraisal of the situation and prompt treatment of the urgent cases are required just where facilities for careful examination and treatment are most difficult to establish and maintain.

It is impossible to give aid to any appreciable number of wounded dying of massive hemorrhage from injuries to the large vessels. A common cause of death that may be relieved even in a first-aid station, however, is pressure pneumothorax. It is reported that deaths occur from the failure to recognize and relieve promptly the suffocation resulting from this complication of penetrating injuries of the thorax. The treatment is as simple as a tracheotomy: the insertion of a cannula between the ribs to provide a vent for the accumulating air.

The hazards of chest-wall wounds that penetrate the pleura and produce a "sucking" pneumothorax are well known. These defects must be closed immediately, either with through-and-through sutures or with an occlusive dressing. Arthur T. Cabot is said to have devised the use of a sheet of rubber dam for this type of occlusive dressing.[44] A more complicated appliance is the inflatable rubber balloon of Morelli.

Injuries that require a formal débridement, with or without the removal of foreign bodies, should be handled as near the front line as facilities for major surgical procedures can be provided. These wounded do not withstand transportation. The dangers of continuing hemorrhage, anoxemia, pressure pneumothorax and pneumonia are immediate and of grave import. A major difficulty lies in the limited number of surgeons trained in the diagnosis and operative technics of endothoracic surgery. An experienced thoracic surgeon can, if circumstances demand it, carry out a débridement of this type without differential pressure anesthesia, as shown by Duval[45] and by Nissen.[46] A surgeon unfamiliar with thoracic mechanics is apt to have his own equilibrium disturbed by the terrifying blasts of air that emerge from the chest and the violent motions of the heart and mediastinum, with the result that débridement is inadequate and the stage is set for infection. Differential pressure anesthesia can be administered with a simple apparatus by means of tracheal intubation, and if this could be made available the surgical problems would be immeasurably simplified. It is believed, therefore, that the management of chest wounds may be materially aided by providing trained anesthetists close to the front. This can be done in a much shorter time than it takes to provide an adequate number of surgeons experienced in chest surgery.

Anatomy of the Lung

The detailed structure of the bronchial tree and the intricate ramifications of the pulmonary blood vessels have become matters of everyday practical importance in the diagnosis and surgical treatment of pulmonary disease. It is impossible to present a résumé of this subject without reference to anatomical sketches and extensive descriptions. For these the reader must consult original sources.[47–50] As in all other anatomical studies, a first-hand knowledge by actual dissections is required to establish an adequate working basis for precise surgery.

The bronchopulmonary segment, from the stand-

point of roentgen diagnosis and surgical dissection, is the gross unit of lung structure. The limits of these segments are sharply marked on the periphery by injection technics, and their relations to the surface anatomy of the chest wall can be defined within approximate limits. Variations in respiratory excursion, changes in the position of the diaphragm and disease processes in the lung itself all tend to distort the normal topography. A bronchopulmonary segment of the lung is also for all practical purposes a vascular segment, since the number and size of vessels crossing segmental lines in the periphery are relatively insignificant. As the hilar region is approached these anastomosing channels occur with increasing frequency.

At the present time there exists some disparity in the terminology used to designate individual bronchovascular segments and tertiary bronchi. The anatomic pattern itself, however, is far more constant than was formerly believed.

Esophagus

A complete review of recent advances in the surgery of the esophagus has been compiled by Bird[51] and has been published with an appended bibliography of 677 references. There is no reason to add further comment regarding this important phase of thoracic surgery. It is well to bear in mind the fact that progress is being made in the hitherto discouraging field of carcinoma of the esophagus, and that every clinic which is concerning itself with the surgical treatment of this disease is collecting an impressive series of encouraging results.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 26411

PRESENTATION OF CASE

First Admission. A sixty-four-year-old white widow entered the hospital complaining of weakness, apathy and loss of weight.

The patient had been vigorous and healthy until four years prior to admission, when she began to suffer from exhaustion. She had swollen "glands" in the neck with a high temperature. After two months in bed and rest in the country she improved somewhat. She entered an outside hospital for study and was treated for hypothyroidism, requiring 12 gr. of thyroid daily at first, later 2 gr. She was operated on for tuberculous lymph nodes in the neck. One year before admission she had another lymph node of the neck removed. Six months later she entered a Boston hospital where a complete study was essentially negative. Insulin therapy to help her put on weight was immediately followed by rather severe reactions. Soon after this, she complained of shortness of breath, exhaustion and stiffness in the back of the neck. There was a loss of weight of 16 pounds during the last year. She had no appetite and complained of a burning sensation in the right upper quadrant. Her daughter stated that she had no interest in anything, and that she would sit for long periods of time hardly talking or moving. She did not sleep well. She had had the menopause at the age of forty-eight. The diet was very meager in every respect. The past history revealed that she had had "peritonitis" thirty years before admission. One brother died at forty-five of "a neglected cold."

Physical examination by her physician about five months before entry showed a poorly developed and markedly undernourished apathetic woman. There was a yellowish color to the skin. Examination of the head was negative. The thyroid gland was normal to palpation. The chest was normal except for diminished expansion on the right. The systolic blood pressure was 80; the diastolic could not be read. The breasts were normal. Abdominal examination was negative. There was no edema, but the left leg appeared to be larger than the right. The knee jerks were active, but the right appeared to be somewhat more active than the left.

The urine was negative except for an occasional hyaline cast. The blood showed red-cell counts ranging from 4,500,000 to 5,500,000, and a white-cell count of 9800 with 51 per cent polymorphonuclears, 39 per cent lymphocytes, 6 per cent mononuclears and 1 per cent eosinophils. The total base in the blood was 146.5 milliequiv. per liter, and the sodium 137.8 milliequiv. The serum protein was 5.7 gm. per 100 cc.

Her physician prescribed a full diet, graded exercise, and three 15-gr. capsules of sodium chloride with each meal. She improved for a while and gained a slight amount of weight, and the blood pressure rose to 117 systolic, 85 diastolic. When she began to follow her regime less strictly, her condition became less satisfactory. She was then sent to a nursing home, where thyroid, yeast, salt and amphetamine were given. She showed marked improvement, but after a few weeks, she again began to fail.

Physical examination on entry showed an undernourished woman weighing 90 pounds. Examination of the head and chest was negative. The blood pressure was 100 systolic, 80 diastolic. The abdomen was normal.

The temperature was 98.6°F., the pulse 60, and the respirations 20.

Examination of the urine showed a specific gravity of 1.010, a trace of albumin, and no sugar, acetone or bile; there were 25 white cells per high-power field, with frequent small clumps. A urine culture showed staphylococci and a few colon bacilli. There was no follicle-stimulating hormone (prolan A) in the urine. The blood showed a red-cell count of 4,250,000 with 80 per cent hemoglobin, and a white-cell count of 9800 with 56 per cent polymorphonuclears, 25 per cent small lymphocytes, 17 per cent mononuclears, 1 per cent eosinophils, 1 per cent basophils; the smear was normal. The fasting blood sugar was 84 mg. per 100 cc. The basal metabolic rate was −17 per cent. A stool examination was negative for fat.

X-ray films of the skull showed that the bones of the vault were rather heavy and dense. There was some increase in vascular markings on both sides, but there was no evidence of increased intracranial pressure. The sella turcica was normal in size and shape. The pineal gland was calcified and in the normal position. There was no definite evidence of intracranial disease. Plain films of the abdomen were negative.

Pituitary injections and thyroid, salt and vitamin therapy were given. She was discharged on the seventh hospital day.

Final Admission (one week later). Following discharge the patient had run a steady downhill course. Physical examination was essentially un-

changed except for more marked weakness and emaciation. The temperature was 102.5°F., the pulse 65, and the respirations 20. The urine showed a large trace of albumin and innumerable white cells. The blood showed a red-cell count of 4,000,000 with 70 per cent hemoglobin, and a white-cell count of 12,300. Terminally she went into coma. The blood pressure dropped to 75 systolic, 0 diastolic. The temperature rapidly rose to 106°F., and she died on the third hospital day.

Differential Diagnosis

Dr. Alfred O. Ludwig: This is the story of a sixty-four-year-old woman who was apparently suffering from some disease that caused her progressively to lose strength and weight, and also to become apathetic and somewhat depressed. The first thing of interest is the history of swollen lymph nodes in the neck. I do not know whether they were proved to be due to tuberculosis, but one would be led to think so. One is told that she was operated on for tuberculous glands of the neck, although we do not know whether it was a postoperative or preoperative diagnosis. At the same time it was thought that she had thyroid deficiency because of the low metabolic rate, and possibly because of other signs. She then had recurrent attacks of difficulty with the lymph nodes in the neck and had to be operated on again.

Another interesting point is that the administration of insulin was immediately followed by a rather severe reaction. That could take place in a number of different conditions. Such insulin reactions occur in patients who are emaciated and have lost weight from any cause, but particularly in those who have deficiency of the anterior lobe of the pituitary gland, or of the adrenal cortex.

The symptoms of shortness of breath on exertion, stiffness in back of the neck, and loss of weight do not help much in classifying the disease from which the patient was suffering. There is no evidence that she had tuberculosis elsewhere except in the neck. There is nothing here to tell us what was the nature of the peritonitis thirty years before. We do not know what happened to her brother; the "neglected cold" may have been pulmonary tuberculosis, but we have no way of knowing that.

Physical examination five months before she came into the hospital showed only loss of weight and a diminished expansion on the right side of the chest. These symptoms may mean old pulmonary tuberculosis with some fibrosis on the affected side. The left leg appeared to be larger than the right. I do not know what this means. The left leg may have appeared to be larger than the right because of atrophy of the muscles on the latter side; possibly there was a thrombophlebitis on the former side to account for the slight increase in size. I am inclined to discount the information about the knee jerks being more active on the right side than on the left, because we have no evidence of the presence of any other abnormal reflexes on the right side which might lead us to suspect a neurologic disturbance.

There was no significant anemia at this time. The smear and white cells appeared to be within normal limits. Apparently a diagnosis of adrenal insufficiency was suspected because determinations of total base and sodium were carried out. All these levels are a little low, but still within normal limits. The low serum protein might be accounted for on the basis that the patient had been on insufficient intake of protein. Treatment was prescribed with a diagnosis of adrenal insufficiency in mind, and the patient was given sodium chloride. We have no information as to whether she was given adrenocortical extract, but she did seem to improve somewhat, with a slight gain in weight and an increase in blood pressure. This improvement did not last very long, however. The patient continued to lose weight, and the blood pressure again fell.

On the next admission evidence of urinary infection appeared. The most important statement I have so far noticed is that there was no follicle-stimulating hormone in the urine. In women past the menopause there is an increase in this hormone in the urine which persists throughout life. I should say that this was an extremely important finding which in this case might point, and I think does point, to a disturbance of the anterior lobe of the pituitary gland. On this admission the patient showed a slight anemia which was normochromic in type, as confirmed by the normal smear. The white-cell counts were within normal limits. She had a low blood-sugar level and a low basal metabolic rate at that time. Apparently there was no pancreatic hyposecretion, at least insofar as fat metabolism was concerned, as shown by the absence of free fat in the stool. I wonder if we might see the x-ray films at this time.

Dr. Richard Schatzki: The roentgenograms of the skull are not here. The only ones we have are two flat films of the abdomen, which show no unusual mass. There are two areas of calcification on the left side. One could conceivably be in the adrenal gland, but with the other present at the same time I doubt if either is in the gland. They are possibly in the spleen or lower portion of the lung behind the diaphragm. Otherwise there is nothing that would interest you; just changes due to age.

DR. LUDWIG: What about the condition of the bone? Is there any evidence of decalcification?

DR. SCHATZKI: How old was the patient?

DR. LUDWIG: Sixty-four.

DR. SCHATZKI: There is evidence of sclerosis and of degenerative changes of the lumbar spine, but if I had to judge the age of the patient by looking at the bones I believe I could come out quite accurately.

DR. LUDWIG: There is no evidence of decalcification?

DR. SCHATZKI: Not an unusual amount.

DR. LUDWIG: It sounds as though the patient always had this type of skull. I interpret the final episode as being caused by progressive urinary infection with increase in temperature and finally coma and death. The main problem narrows itself down to the cause of this woman's loss of weight and general emaciation, low blood pressure, low metabolic rate, low blood-sugar level and abnormal sensitivity to insulin. Almost all these findings occur in the presence of adrenal insufficiency, but I should think that if she had adrenal insufficiency for this length of time, this woman would probably have had pigmentation of the skin and mucous membranes which, so far as we know, was not present. All the other findings would be perfectly consistent with adrenal insufficiency. I do not know about the absence of prolan A in the urine, but I do not believe this occurs in adrenal insufficiency. On the other hand, an insufficiency of the secretion of the anterior lobe of the pituitary gland could also cause all these phenomena, because this gland contains a very large number of hormones — I think there are about ten now. One is prolan A; another, thyrotropic hormone, the absence of which might be responsible for the lowering of the metabolic rate; another, an adrenotropic hormone, the absence of which might be responsible for some of the symptoms referable to insufficiency of the adrenal gland; and another, a parathyrotropic hormone, in the absence of which there might be some changes in the bone. Loss of secretion of the anterior lobe might well be responsible for all the disturbances in this case. In addition, increased sensitivity to insulin is well known in cases of pituitary insufficiency, particularly in Simmonds's disease. The cases that Simmonds[1] described usually occur in women shortly after the puerperium, and were due to embolism or thrombosis of the nutrient artery of the pituitary gland, with secondary atrophy of the gland. So far as we know this woman certainly had no active thrombophlebitis in the course of her illness. On the other hand she did have tuberculous lymph nodes in the neck with secondary infection and terminal urinary infection, but I do not think that these played a part in any changes that might have taken place in the pituitary gland.

I believe that the patient did have an insufficiency of the anterior lobe of the pituitary gland, probably secondary to atrophy, the cause of which I do not know. Whether it was due to tuberculosis or to vascular changes with disturbances of circulation and nutrition of the gland I have no way of determining. I do not believe that she had Addison's disease.

DR. ROBERT S. PALMER: I saw the patient during the last year of her life and made tentative diagnoses of involutional melancholia and adrenal insufficiency. She had progressive loss of weight and strength, and went steadily downhill with more gastrointestinal symptoms than are indicated here. In spite of the fairly normal blood chemical findings I therefore made a tentative diagnosis of Addison's disease. The patient also had the benefit of stays at two sanatoriums, but did not improve. She never responded to psychotherapy.

DR. FULLER ALBRIGHT: The differential between Addison's disease and Simmonds's disease may be extremely difficult. Many of the manifestations of Simmonds's disease are due to secondary adrenal insufficiency. I saw this patient and came to the same conclusion that Dr. Ludwig came to, for the same reasons. There was perhaps one fallacy in our reasoning, though, which I have thought of since. Both he and I put emphasis on the fact that there was a negative test for follicle-stimulating hormone in the urine after the menopause. Since this test is normally positive after the menopause, the inference was that there was some deficiency of the pituitary gland. I am not sure, however, that you would get a positive test for follicle-stimulating hormone in a patient with Addison's disease and malnutrition after the menopause. The latter in itself inhibits the pituitary gland.

DR. J. H. MEANS: A great many points in this case have interested the members of the Thyroid Clinic. I agree with Dr. Ludwig that this woman had sufficient evidence to make a diagnosis of hypofunction of the anterior lobe, which in turn brings about a certain degree of hypothyroidism, hypogonadism and hypocortinism, probably all secondary to the anterior-lobe dysfunction. I should like to mention that Richardson[2] pointed out the resemblance of anorexia nervosa and Simmonds's cachexia. I think that the pituitary gland, though not actually diseased, may underfunction because of malnutrition. It is very difficult to say which is the cause in any given patient.

Another point that deserves comment is the statement that the patient received 12 gr. of thyroid. That is an excessive dose. Either it was not absorbed or else she did not get it, because such a dose ought to make her desperately ill. We have had several cases.

For example, one was that of a woman who years ago had had toxic goiter and had made a good recovery under x-ray treatment. Some years later she came in with symptoms of fatigue and showed a low basal metabolic rate. She improved markedly on small doses of thyroid. A number of years after that she was seen for a third time with similar symptoms. Thyroid was again ordered. After taking it for a short while she went into a state of collapse and was brought into the hospital. Study disclosed that she was in a state analogous to the crises in Addison's disease. Indeed, it turned out that she had Addison's disease and that the thyroid treatment had thrown her into the crisis. She was rescued by means of salt and cortin, but later at home — not having followed directions — she went into a second crisis and died.

We also had a woman of twenty-four who was sent into the hospital with a diagnosis of myxedema, in which we concurred. She was placed on thyroid, but in a few days went into a crisis similar to that of the patient just mentioned, from which she too was successfully rescued by salt and cortin. Our conclusion in this case was that she had a pituitary type of myxedema, secondary to anterior-lobe dysfunction, and although thyroid benefited the secondary hypothyroidism, it broke down the adrenocortical function and precipitated a crisis.

When one sees a patient with myxedema who is responding badly to thyroid, one should consider the possibility of anterior-lobe hypofunction. Such people do not tolerate thyroid well until they are protected against hypofunction of other glands by suitable substitution therapy.

The story that 12 gr. of thyroid was borne by the patient is a very puzzling fact; that is to say, if it is a fact.

Dr. Palmer: That happened before I saw her. She improved greatly when she was taking thyroid for four or five months.

Dr. Tracy B. Mallory: I think there must have been a mistake in the recording of the dosage.

Clinical Diagnoses

Simmonds's disease?
Cystitis.

Dr. Ludwig's Diagnoses

Hypofunction of anterior lobe of pituitary gland.
Urinary infection.

Anatomical Diagnoses

Tuberculosis of the adrenal glands (Addison's disease?).
Atrophy of the anterior lobe of the pituitary gland, thyroid gland, parathyroid glands and ovaries (Simmonds's disease).
Cholelithiasis.
Salpingitis, chronic, left.

Pathological Discussion

Dr. Mallory: At autopsy we thought we were going to have difficulty in confirming the diagnosis of Simmonds's disease, because we found both adrenal glands were caseous and it seemed as if we must be dealing with Addison's disease. However, on further investigation, the thyroid gland weighed only 3½ gm. and the pituitary gland was composed mostly of posterior lobe. Shrunken, atrophied and scarred, the anterior lobe showed almost complete absence of basophilic cells, so I think there is no doubt that it really was Simmonds's disease. Outside of the endocrine system the only findings were terminal pyelonephritis, — which I do not think was very important, — chronic, non-tuberculous salpingitis and cholelithiasis.

Dr. John H. Talbott: How much normal cortical material remained?

Dr. Mallory: Roughly one tenth.

Dr. Talbott: We have the impression that to produce typical Addison's disease the cortical tissue must be reduced to a very low percentage of normal and that some of these patients can carry on with only one fifth or one tenth of the usual amount of cortex.

Dr. Mallory: I think I have seen adrenals with about this amount of cortical tissue left in patients who did not have Addison's disease.

Dr. Means: What do you think the sequence of events was?

Dr. Mallory: I cannot tie them together. I do not believe the lesion in the pituitary gland was tuberculous. There was nothing to suggest it.

Dr. Albright: You do not believe she had Addison's disease?

Dr. Mallory: I do not, although I cannot be dogmatic.

Dr. Talbott: I did not see this patient at any time during her illness but remember having discussed the diagnosis with Dr. Palmer when she first came under his care. There were many points

in the history, the physical findings and laboratory data that suggested adrenal insufficiency. The subsequent course under his care confirmed this presumptive diagnosis. Absence of pigmentation was against a diagnosis of primary adrenal insufficiency, that is, Addison's disease, and in my opinion was consistent with adrenal insufficiency secondary to pituitary hypofunction. Up to the time of necropsy, this explanation seemed most reasonable. The findings of caseous adrenal glands in addition to pituitary and thyroid atrophy were most unexpected. This is my first encounter with such a combination. My interpretation of the case in the light of these findings would be primary adrenal insufficiency from tuberculous adrenal glands, secondary pituitary atrophy, and subsequently thyroid atrophy. With this interpretation, the pathologic processes could account for the whole clinical picture in logical sequence. The alternative explanation, that is, pituitary hypofunction and coincidental caseous adrenal glands, seems less likely.

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CASE 26412

PRESENTATION OF CASE

A thirty-one-year-old Swedish housewife entered the hospital complaining of fever and generalized aches and pains of ten months' duration.

At eighteen years of age, during a physical examination for life insurance, the patient was told that she had a heart murmur. This was not considered serious enough to bar her from obtaining a policy. Ten months before admission she noticed a constant dull ache in the lower three or four ribs of both sides of the chest, which was not related to respiration. In addition there was a constant ache in the lower thoracic vertebrae, which was not related to movement or position. These symptoms were accompanied by malaise, anorexia and loss of weight. A month passed, and she finally saw her physician who made a diagnosis of rheumatic fever. He kept her in bed for the next ten weeks and prescribed sodium salicylate tablets, and oil of wintergreen to the affected parts. The pain was relieved immediately, but she still suffered from anorexia and general malaise, lost 10 pounds in weight and ran a fever of 99 to 100°F. for nine weeks. For the next few months she felt fairly well, but fatigued easily and frequently noticed that her heart palpated and that she was dyspneic on climbing stairs. From time to time her heart "skipped" a beat, and she had frequent night sweats. Ten weeks prior to entry she "caught cold" and had frequent chills, a temperature of 102°F. and a nonproductive cough; her ribs again became tender. She was given salicylates by her physician; the rib pain immediately disappeared, but the fever remained. Salicylates were increased to the point of emesis with no effect on the temperature, so they were discontinued for four days and then reinstituted in small doses and continued until two weeks before entry. The patient was then given 5 gr. of sulfanilamide five times a day for five days, with no beneficial results. During these five days the patient noticed a pain in the lower left chest in the region of the tenth and eleventh ribs; she described it as a "grating" sensation, increased by breathing and coughing, which frequently forced her to catch her breath.

Although joint pain had been absent, transient soreness and tenderness had occurred in the arms, fingertips and legs. About one month before entry a small subcutaneous lump appeared over the second left chondrosternal junction, which remained for about four days and then disappeared. Her physician said that this was a rheumatic nodule. She had had amenorrhea for the past two months. An Aschheim–Zondek test was negative.

At the age of two years the patient had had "malaria fever," according to her physician, and at ten, severe "flu," with epistaxis which lasted three weeks. She had also had the usual childhood diseases.

The family history was essentially noncontributory. The patient's husband and two children were alive and well.

Physical examination showed a well-developed and well-nourished woman, flushed but not in acute distress. A diffuse, regular, heaving impulse was seen over the precordium, and the apex of the heart was felt in the fifth interspace 10.5 cm. to the left of the midline. A systolic thrill was just palpable at the apex. A loud blowing systolic murmur was heard over the entire left chest. It was loudest at the apex and transmitted into the axilla and left back. The blood pressure was 136 systolic, 62 diastolic. The circumpatellar tissues of the left knee joint were slightly thickened, but there was no crepitation or restriction of movement.

The temperature was 99.6°F., the pulse 132 and the respirations 22.

Examination of the blood revealed a red-cell count of 4,490,000 with a hemoglobin of 74 per cent, and a white-cell count of 14,250 with 78 per cent polymorphonuclears. The urine showed a + test for albumin, an occasional red blood cell, 8 to 12 white blood cells and an occasional granu-

lar cast per high-power field and no bacterial growth. A blood Hinton test was negative.

X-ray films of the chest showed the transverse diameter of the heart to be 12.7 cm., with a chest diameter of 23.9 cm. The heart appeared slightly enlarged in the region of the left ventricle, and there was a questionable enlargement of the left auricle. The hilar shadows were not increased. Electrocardiographic recordings showed a normal rhythm with a rate of 105, a PR interval of 0.16 second and some somatic tremor.

The salicylates, which the patient had been getting almost continuously, were stopped; the temperature immediately rose, and stayed up even after salicylates were re-instituted. A blood culture at this time yielded 73 colonies of alpha hemolytic streptococci per cubic centimeter. Sulfapyridine therapy was started, but in nine days, when the blood level had reached 10.7 mg. per 100 cc., she developed crampy abdominal pain, hematuria and albuminuria, and the urine contained many sulfapyridine crystals. This treatment was stopped for a week and then continued in smaller doses, but with the same results. Sulfathiazole therapy for a week produced no beneficial results, but led to nausea and abdominal distress. The patient was then given three single days of continuous-drip neoarsphenamine therapy, spaced four days apart; the daily dose was 1 gm. For two weeks during and following this period the blood culture became negative, for the first and last time. Starting a week later the patient was given heparin for seven days, followed by three days of continuous-drip neoarsphenamine therapy and three days of neoarsphenamine and heparin therapy. The heparin was then continued for one week. She tolerated this intensive treatment well, but three days after the last administration of neoarsphenamine she developed paresthesia and numbness of both feet. These symptoms gradually became worse, and in two weeks a severe polyneuritis had developed, with wrist and toe drop, glove-and-stocking anesthesia, absent reflexes, weakness of the muscles of the extremities and bladder hypotonia. An unsuccessful attempt had been made to prevent this complication by the use of thiamine hydrochloride. There were few embolic phenomena throughout her illness, but those that occurred were as follows: one week after admission small red points appeared in the palpebral conjunctiva of both lower eyelids, and a fingertip became sore, with no visible petechiae; eleven days later a tender indurated area could be felt in the left palm. About two months after admission the left ankle on its dorsal aspect became painful and tender, and movement of the joint was limited; the spleen could be felt for the first time.

With the establishment of the severe peripheral neuritis the patient pursued a gradual downhill course. Liver-function and kidney-function tests were normal on the completion of chemotherapy. During the last month of her illness the patient developed a cystitis, then diarrhea; hemorrhages appeared in the conjunctivas and fundi. About seventeen weeks after admission she complained of a sudden blurring of vision and a "funny feeling" in the back of the head. She lapsed into coma, and died ten hours later.

Differential Diagnosis

Dr. Edward F. Bland: Usually in these conferences the discusser is expected to review the clinical data as given and to arrive at certain reasonable conclusions in regard to the cause of the patient's illness and death. The pathologist then checks us up. It seems to me that here we are not given much choice as to the differential diagnosis, for this record is almost a textbook recital of the classic manifestations of subacute bacterial endocarditis. In addition there are at least two groups of symptoms related more directly to the therapeutic agents employed than to the disease itself.

In the first place we probably have adequate evidence to suppose that minimal valvular disease preceded the appearance of the final infection. The mitral valve apparently had been scarred since childhood, and one or both of the two earlier illnesses may have been rheumatic fever. I am especially suspicious of the one labeled "flu," which lasted three weeks and was associated with nosebleeds. The patient did well thereafter and presumably had very little residual damage to the heart. We have no evidence of subsequent rheumatic activity, although this possibility must, or should, have been tentatively considered at the onset of the final illness, ten months before death, and before the results of the blood cultures were known. There are one or two points, however, even earlier in the illness that are rather strongly against rheumatic fever. The story of recurring chills is most unusual in rheumatic fever — chills sometimes occur but certainly they are extremely rare. The nodule for which a rheumatic origin was considered appeared rather quickly and disappeared in three or four days. Its transient nature, its location and the absence of similar nodules elsewhere are points against its rheumatic origin. I believe that it must have been an embolic phenomenon. Another point might legitimately be raised, as apparently it was, namely, the relief from salicylate therapy noted early in the record. We now know that the response to salicylate therapy is not quite so specific in rheumatic fever,

as opposed to that in other rheumatic and febrile diseases, as we had once thought. Therefore, in view of the very complete and convincing data here recorded, it is difficult to consider any possible diagnosis other than subacute bacterial endocarditis superimposed on minimal rheumatic scarring of the mitral valve.

The signs in the heart — the loud apical systolic murmur and the fullness of the left auricle in the x-ray films — indicate mitral regurgitation. This type of valvular deformity is very prone later to become the site of secondary bacterial infection. Aortic valves that regurgitate are also likely to be the site of bacterial endocarditis, as are almost all types of congenital defects in the heart. I think we must keep the bare possibility in mind that there was a slight congenital defect rather than rheumatic mitral regurgitation; but the prominence of the left auricle is fairly good evidence of previous scarring of the mitral valve, and the absence of emboli to the lungs negates a congenital septal defect or a patency of the ductus. Although only one of the blood cultures is specifically mentioned as being positive, it is said later that they were sterile only for a period of two weeks. We must therefore assume that there were many positive blood cultures for the same organism.

Next we come to the therapy. Whatever else one may say, I think we shall all agree that a very determined effort was made to combat the progress of this fatal infection. It is interesting to mention briefly a few of the renal complications following the use of the newer chemotherapeutic agents. Sulfapyridine crystals are not infrequently precipitated in the urine, particularly that in the renal pelvis or bladder, so that the symptoms therefrom are inclined to simulate "gravel" in the urine. The deposition of crystals of sulfathiazole, however, appears to take place in the renal tubules; hence the clinical picture is apt to resemble that of diffuse glomerulonephritis. In this case it is reasonable to assume that the gross hematuria and albuminuria were largely the result of sulfapyridine therapy.

Then we come to a second complication which I think was caused by the therapy and not by the disease itself, namely, the severe polyneuritis. I have not personally observed polyneuritis, nor can I find a record of such as a result of subacute bacterial endocarditis. Perhaps in patients as sick as this woman was it might rarely occur, but it has apparently not been described. On the other hand, polyneuritis is not unusual after the use of heavy metals. In this case I am inclined to attribute it to the presence of a heavy metal, namely, arsenic. Why was neoarsphenamine used? Arsenic has been recommended for many years in one form or another as an agent to combat this infection. More recently a physician on the Pacific Coast has apparently had some success using it in a constant drip intravenously. I am not certain whether or not he has combined it with heparin. Perhaps he has, and I suspect that his results were in part responsible for the trial of the combined therapy in this case. It is not so stated, but I should like to ask whether this patient received sulfamethylthiazole prior to the appearance of the polyneuritis. We have seen peripheral neuritis after sulfamethylthiazole, but not after sulfanilamide, sulfapyridine or sulfathiazole. If the patient had received sulfamethylthiazole, it would add another agent that might have precipitated the polyneuritis. The spleen in the meantime became palpable. One wonders a little if the fingers also became clubbed, since that is about the only one of the classic signs of subacute bacterial endocarditis that is not specifically mentioned.

Finally, we come to the terminal few hours of this patient's life. Patients severely ill with this disease not infrequently lapse into coma before death. On the other hand, emboli arising in the heart and going to the brain, as well as to other parts of the body, are very common, in fact almost an essential feature of the disease. Following the institution of heparin therapy in this hospital there seemed to be an increase in the incidence of subarachnoid hemorrhage. But I have seen two patients with subarachnoid hemorrhage as a terminal event, neither of whom had received heparin. I consequently believe that in the beginning there was a slight overemphasis on heparin as a precipitating factor in cerebral hemorrhage. Perhaps, however, this still remains a real hazard. The fact that this patient did not develop paralysis is a little against a localized thrombosis or embolus — the head discomfort followed by dimness of vision and coma is more suggestive of subarachnoid hemorrhage. I suppose that, by the law of chance, cerebral infarction was the most likely, perhaps precipitating more extensive bleeding in the subarachnoid space. I conclude then, that this patient had chronic rheumatic heart disease, with scarring of the mitral valve, superimposed subacute bacterial endocarditis and a terminal subarachnoid hemorrhage.

Dr. Paul D. White: It was during my term of general medical ward visits that this young woman entered the hospital. She looked surprisingly well for a person with a history of long illness, and there was not any clear indication at that time of subacute bacterial endocarditis, although, as Dr. Bland pointed out, her illness did not quite fit with

a diagnosis of rheumatic disease. I believe that she had acute rheumatic fever superimposed on chronic rheumatic heart disease with mitral valve deformity but that subacute bacterial endocarditis had to be ruled out. It was not ruled out but was ruled in very quickly by positive cultures — she was practically never free of these from the onset. It was still during the year of our experimental trials with chemotherapeutic agents, and we started off with sulfapyridine and then gave sulfathiazole. About two months before the patient died, there were three interesting comments. Dr. Mead wrote, "It looks as though we are licked," and I agreed with that. A few days later I wrote, "Review of the course of illness in the last few weeks makes me think that the chemotherapy, particularly with sulfapyridine, has had a somewhat retarding effect on the infection, but not enough in view of the toxic effects; for that reason I do not advise heparin." Even then we realized that unless we got a favorable effect from the original drugs, sulfapyridine or an allied chemical, we could not expect much benefit from its combined use with heparin or from heparin alone. I also wrote: "Perhaps the new drug, sodium paranitrobenzoate, may be available for the patient before it is too late." Was it given to this woman?

Dr. Sedgwick Mead: No.

Dr. White: It has not proved of any value in the few cases we have treated with it.

All subsequent attempts to stem the tide in this case were futile. During the next two months we did not use chemotherapy, but evidently neoarsphenamine was subsequently given, with toxic effect. I do not believe sulfamethylthiazole was used. She was, as I view her now, an unfavorable case almost from the start. There was little control of the infection, the temperature never came down to normal, and the blood was free from bacteria for only about two weeks.

A Physician: That might have been due to the bacteriostatic effect of drugs.

Dr. White: Only the cases that respond quickly and strikingly to initial treatment are likely to have a fair outlook. In such cases heparin as additional therapy may be worthwhile on theoretical grounds. We have noted very little harm from heparin, but definite untoward effects from such drugs as sulfapyridine and neoarsphenamine. Clinical work on the Pacific Coast in the use of neoarsphenamine and experimental work in vitro and in animals stimulated us to try the drug in a few patients, but we have had no luck with it. A few more favorable results have come from the combined use of sulfapyridine and heparin. Heparin was not responsible for the hemorrhage in this case, because that drug was not being administered during the last few weeks of the patient's life. There is no prolonged effect on the clotting time by heparin after it has been withdrawn, and several other cases of subacute bacterial endocarditis not receiving heparin have had cerebral hemorrhages, as Dr. Bland has stated. Although heparin is likely to increase the probability of hemorrhage in the face of embolism, it is not commonly the cause of hemorrhage in these patients.

Clinical Diagnoses

Subacute bacterial endocarditis.
Cerebral embolism.

Dr. Bland's Diagnoses

Chronic rheumatic heart disease.
Mitral regurgitation.
Subacute bacterial endocarditis.
Subarachnoid hemorrhage.

Anatomical Diagnoses

Subacute bacterial endocarditis, mitral valve.
Endocarditis, chronic rheumatic, mitral valve.
Cerebral hemorrhage, with rupture into lateral ventricle and Sylvian fissure.
Subarachnoid hemorrhage.
Infarcts of spleen and kidney.
Embolic nephritis.
Miliary infarcts of the myocardium.

Pathological Discussion

Dr. Benjamin Castleman: This case was inserted in these exercises to get some discussion of the more recent therapy used in cases of subacute bacterial endocarditis. The patient did have subacute bacterial endocarditis involving the mitral valve. The valve had been previously damaged, as evidenced by the thickened cusps and chordae tendineae, although there was no appreciable stenosis. The vegetations had extended down from the valve edge to the chordae tendineae and up on the auricular wall. There was no involvement of any of the other valves with either rheumatic infection or bacterial endocarditis. The patient also had infarcts of the spleen and kidney, and microscopic examination of the kidneys showed the usual finding of embolic nephritis. The myocardial sections contained many miliary infarcts, a finding that has been emphasized by Buchbinder and Saphir[1] as being a cause of heart failure in bacterial endocarditis. De Navasquez,[2] on the other hand, found these lesions in 95 per cent of his cases but believed there was no relation to heart failure.

DR. WHITE: Were there any renal calculi?

DR. CASTLEMAN: No.

The brain was quite interesting. There was a subarachnoid hemorrhage caused by the rupture of a large cerebral vessel into the Sylvian fissure. It had also ruptured into the lateral ventricle. I was under the impression that this hemorrhage was due to heparin, but it apparently had not been given to this patient for a long time.

DR. MEAD: She had not had heparin for the three weeks before death, and its effect wears off very quickly.

DR. CASTLEMAN: Perhaps it is only coincidental, but it is interesting to note that during the past year or so we have had about half a dozen cases of subacute bacterial endocarditis with massive cerebral hemorrhage—a finding that was very rare before the days of chemotherapy.

DR. WHITE: Two other facts should be mentioned. First, this patient with a relatively slight amount of disease in the mitral valve represents the type of case we encounter most commonly with this complicating disease. Secondly, it is just beginning to be realized that there is a wide range of strains of *Streptococcus viridans,* each one reacting differently to these various drugs; until more work is done in differentiating the reaction of the specific organism to the specific chemotherapeutic agent, we are not going to get very far in any particular case.

A PHYSICIAN: I should like to add that in a New York hospital where intensive arsenic therapy for syphilis has been carried out peripheral neuritis is a fairly frequent complication.

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E PLURIBUS

Not long ago a highly respected newspaper commented editorially on the hypothesis that America had at last completed its long retreat from illusionment.

A number of facts seem to give support to this statement. We no longer place reliance on our ocean boundaries or the continued effective goodwill of our neighbors. We are no longer confident in the practical value of our man power, untrained and unarmed; we have come suddenly to realize that soft gold is a base metal until the modern alchemist's touch has converted it into the tough steel of defensive armaments.

This conversion of our currency has commenced. We have voted vast appropriations for naval increase. So far as anyone knows we are building planes on a constantly increasing scale of production. The American Medical Association has already started to organize the medical profession. We have almost enthusiastically supported Congress in a decision that is revolutionary and formerly undreamed of in this democracy — the passage of a conscription bill with the country officially at peace. We are almost pathetically eager that somehow our ramparts should be watched.

And yet with all this talk and activity one can sense beneath the surface a feeling of unreality; as if we truly believed it all to be an uncomfortable dream, from which we shall awaken to plod along again in our comfortable middle-class fashion, concerned over our customary problems, but quite sure that we shall be getting up from the same bed in the same house for some time to come, with a hot breakfast ready on the table.

Despite our financial panics and our economic depressions, our worries over the price of veal chops and our personal, medical agitations concerning colored crosses and governmental interference with the practice of medicine, we have got along fairly well, and we do not want the affairs of the world to disturb us. We have reached that danger point in the history of a nation where an increasing gold reserve is balanced by a declining birth rate; where the accumulation of wealth may soon go hand in hand with the decay of man.

A common danger to which we shall eventually become fully awake, a retreat from illusionment which may soon be completed, a common cause in which our country will again become united may yet prove to be our moral, political and economic salvation. But regardless of what may happen on the face of the earth in the next few years, of one thing we can be certain. The world is going to be a tougher place in which to live than it has been for generations, and free men must be as tough to hold their places in it as they once were to win them.

Men now living will not again walk down the primrose path of the last few decades, and in this fact, too, may come salvation.

SURGICAL CATGUT *U.S.P.*

Over eight years ago the deplorability of the lack of standards or regulations to ensure the sterility of surgical catgut was commented on editorially[1] in the *Journal*. At that time it was suggested that the National Institute of Health, the laboratory of the United States Public Health Service that so effectively guarantees the potency and sterility of biological products subjected to interstate distribution, was the logical agency for control. During the subsequent years, however, little occurred, other than a gradually, although slowly, increasing appreciation by hospitals and surgeons that the so-called "sterility" of such sutures, unless controlled by the method recommended by Meleney and Chatfield,[2] meant nothing and that the use of sutures other than those tested by this method was hazardous.

Some action has at last been taken, and the *Second Supplement* of the eleventh decennial revision of the *United States Pharmacopoeia* establishes standards for surgical catgut, the development of which was made possible through the establishment of the Sterile Products Advisory Board, with the co-operation of various interested parties. These include tests for sterility,—as recommended by Meleney and Chatfield, revised by Clock[3] and used by Brewer,[4]—for tensile strength and for length and diameter. No test for absorption is presented, but it is specified that tanned catgut or that otherwise treated to resist digestion shall carry the notation "mild treatment," "medium treatment" or "prolonged treatment," depending on the duration of the procedure. These standards become official on January 1, 1941, and thereafter all catgut intended for surgical use must, according to the Food, Drug and Cosmetic Act, meet the requirements. Any product failing to conform must be labeled in such a way as to indicate in every respect the manner in which it differs.

The omission of a standard for absorption is regrettable but wise, for no test has yet been devised that serves as an adequate measure of this property. Tests for absorption in animals are not necessarily applicable to the results in human beings. The Advisory Board is favorably impressed by in vitro tests using trypsin as the digestive solution,[5] but there are various factors that must be controlled before this method will become a reliable test of absorption. This one property—so important in the reduction of the dangers due to hemorrhage or leakage and in the incidence of wound disruption—must, for the moment, remain unstandardized, other than for the previously mentioned requirement that the time of processing be specified. A forward step has been taken, however, and the surgeon can at least be assured of a sterile product of accurate length and size and of suitable tensile strength.

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MEDICAL EPONYM

Ehrlich's Diazo Reagent

"Ueber eine neue Harnprobe [A New Urine Test]" is the title of an article by Professor Paul Ehrlich (1854–1915) which appeared in the *Zeitschrift für Klinische Medicin* (5:285–288, 1882). A portion of the translation follows:

> The diazo groups, which are produced by the reaction of nitric acid on the amido groups of the aromatic series, have the ability, as is well known, to combine with a large number of substances, particularly the mono-, di- and poly-phenols as well as the primary, secondary and tertiary mono- and di-amines of the aromatic series, with color formation.
>
> This reaction . . . seemed susceptible of medical use. That is, it was to be expected that substances might be present in the secretions and excretions of the human body, but above all in the urine, which would give color reactions with the diazo groups. . . . Indeed my expectations have been confirmed, and these substances have given color reactions in the urine which seem by reason of their significance to be adapted to clinical and diagnostic use. . . .
>
> The solution which I used is prepared as follows: I strongly acidify a moderate amount of water, about 500 cc., with pure nitric acid (30–50 cc.) and add to this enough sulfanilic acid, which is rather difficultly soluble, so that the excess sinks to the bottom. A few granules of sodium nitrite are now dissolved in water in a test tube, and this solution is gradually added, with shaking, to the first. The above-described reagent retains its efficacy, particularly if the weather is not too warm, for some time; it remains useful for two to three days in summer, or as much as five days in winter.

R. W. B.

OBITUARY

AUGUSTUS THORNDIKE

1863 – 1940

Dr. Augustus Thorndike died suddenly on August 23, 1940, at his summer home in Bar Harbor, Maine, at the age of seventy-seven years.

His wife, the former Alice Amory, of Boston, whom he married in 1892, died two years ago. They had five children, who survive him: Mrs. Lyneham Crocker, Mrs. Alexis Sommarina, Dr. Augustus Thorndike, Jr., Charles Thorndike and Robert Amory Thorndike.

He was born in Paris, but his education was received in this country. After graduating from Harvard College in 1884 and from Harvard Medical School in 1888, he served as intern on the Surgical Service at the Massachusetts General Hospital, at the Boston Lying-in Hospital and at the House of the Good Samaritan.

From the beginning of his practice Dr. Thorndike was interested in orthopedic surgery, and until his retirement in 1918 he played an active part in this department of medicine in New England. He was a member of the staffs of the Children's Hospital and of the House of the Good Samaritan, and in addition was associated at times with the Boston Dispensary in the Orthopedic Department and also at St. Luke's Home for Convalescents. At that time a large proportion of the cases were tuberculous, and, since the hospital equipment was much more limited than at present, they required a great deal of careful personal attention from those who were in direct charge. Dr. Thorndike's capacity for conscientious care and the great sympathy which characterized his attention to his patients were evidenced by the success which he had with these difficult cases. As visiting surgeon, he gave a great deal of his time to this work at the House of the Good Samaritan, which was then one of the few institutions providing treatment for such cases, and during all his professional career he was an active member of the staff of the Boston Children's Hospital where his work was characterized by the same conscientious care and sympathy. He was particularly concerned with the problem of the crippled child, in relation not only to medical care but to education and occupational training. He was one of the incorporators of the Boston Industrial School for Crippled Children and was actively interested in the establishment of the State Hospital School for Children at Canton.

He was an active member of many societies in and about his home, — the Massachusetts Medical Society, the Boston Medical Benevolent Society and the Society of Medical Sciences, — and he was also interested in the Boston Medical Library. Dr. Thorndike was a member of the American Medical Association. He was also a member of the American Orthopedic Association, to which he was elected in 1893, and served as its president for the year 1909–1910. He always took an active interest in this association, and the welcome accorded him at the meetings was evidence of the high esteem in which he was held.

Dr. Thorndike was generous in his estimate of his associates, never sparing in his efforts to help, and he gave freely of himself. He had the faculty of bringing out the best in those with whom he worked. He had definite and strong convictions but was always kindly and tolerant toward the opinions of others even when differing from them.

MASSACHUSETTS MEDICAL SOCIETY

THE ONE HUNDRED AND SIXTIETH ANNIVERSARY

The exercises of the one hundred and sixtieth annual meeting of the Massachusetts Medical Society will be held in the Copley-Plaza Hotel, Boston, on May 21 and 22, 1941.

SECTION OF OBSTETRICS AND GYNECOLOGY*

RAYMOND S. TITUS, M.D., *Secretary*
330 Dartmouth Street
Boston

DIABETES AND PREGNANCY IN THE PRE-INSULIN ERA

Mrs. J. R., a twenty-nine-year-old primipara, was first seen on September 15, 1919. She was referred by her family physician because of sugar in the urine.

The family history was non-contributory. The patient's past history included asthma and pleurisy. Catamenia began at fourteen, were regular with a twenty-eight-day cycle and lasted four to five days. The last period began on March 27, making the expected date of confinement January 4, 1920.

Physical examination revealed a thin woman. The heart was not enlarged; there was a systolic murmur at the base. The lungs were clear and resonant; there were no rales. The blood pressure

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

was 120 systolic. Abdominal palpation revealed a uterus enlarged to the size of a four and half months' pregnancy. Vaginal examination revealed a long cervix. There was considerable sugar in the urine, and the patient was referred to a specialist in diabetes.

On September 16 the patient entered the hospital for treatment. On entrance the urine contained 5.3 per cent sugar. The weight was 99 pounds. She was placed on a diet of 50 gm. of carbohydrate, 75 gm. of fat and 46 gm. of protein. The total caloric intake was raised from 700 to 1100. On this diet the amount of sugar in the urine was reduced to a fraction. Fasting blood-sugar determinations were normal — 100, 160 and 100 mg. per 100 cc. The blood-cholesterol level was 167 mg. per 100 cc. There was no albumin in the urine. The blood pressure was 110 systolic, 75 diastolic. A blood Hinton test was negative.

The patient left the hospital on October 3 and was seen in the office on November 1 and again on December 15. On the diet containing approximately 1100 calories the amount of sugar in the urine varied from 0.2 to 0.4 per cent. The blood sugar remained normal. At the time of the latter visit the weight was 120 pounds, a gain of over 20 pounds. She had a considerable amount of edema, but the urine contained only the slightest possible trace of albumin. The blood pressure was 135 systolic, 80 diastolic.

On December 16, the day following the office visit, labor started spontaneously. At this time the patient was approximately thirty-seven to thirty-eight weeks pregnant. She was admitted to the hospital. Labor was simple, and a low-forceps delivery under gas was readily accomplished. The baby was very thin, long and decidedly undernourished, weighing 4 pounds, 15 ounces. The mother made an uneventful convalescence. The baby did well and was discharged well.

While in the hospital the diet, at first, consisted of 62 gm. of carbohydrate, 54 gm. of fat and 64 gm. of protein. This was subsequently raised to 79 gm. of carbohydrate, 107 gm. of fat and 83 gm. of protein, a caloric intake approaching 1600 calories. Upon the latter diet the blood sugar was normal, and the urine sugar-free; the blood pressure was 120 systolic, 80 diastolic. Her weight at the time of discharge from the hospital was 86 pounds. A sugar tolerance test done at this time gave the following values: fasting, 80 mg.; one hour, 160 mg.; two hours, 170 mg. per 100 cc.

On October 17, 1920, the patient was seen by the medical consultant. She had not tested the urine since the previous February. She had had amenorrhea since delivery. The weight was 82 pounds, and she had been eating what she chose. The urine showed 1 per cent sugar, and the blood-sugar level was 260 mg. per 100 cc. She died in diabetic coma a year and a half later.

Comment. This case is illustrative of diabetes in the pre-insulin era. Whether the diabetes existed before pregnancy or developed during pregnancy is unknown. The patient was kept alive on a diet that was barely sustaining, resulting in a very much undernourished infant in contrast to the overnourished diabetic babies seen so frequently at that time and still seen. Like so many other diabetic patients this woman did not go to term but started labor two to three weeks prematurely. Pregnancy undoubtedly did her no good, and even if she had been more conscientious about her diet, the final outcome would probably have been the same.

In the pre-insulin era, diabetic patients who were fortunate enough to become pregnant too frequently delivered themselves of overnourished, macerated infants, and only those whose disease was of moderate severity and who were kept on practically a starvation diet were fortunate enough to give birth to living children. As will be illustrated in subsequent cases, the administration of insulin has entirely changed this picture.

POSTGRADUATE EXTENSION COURSES

The postgraduate extension courses for the academic year 1940–41 will be given in three divisions as follows:

FALL

DISTRICT	PLACE
Barnstable	Hyannis
Bristol North	Taunton
Bristol South	New Bedford
Essex North	Lawrence
Essex South	Salem
Middlesex North	Lowell
Plymouth	Brockton

WINTER

Middlesex East	Melrose
Middlesex South	Cambridge
Norfolk	Norwood
Norfolk South	Quincy
Suffolk	Boston
Worcester	Worcester

SPRING

Berkshire	Pittsfield
Bristol South	Fall River
Franklin	Greenfield
Hampden	Holyoke, Springfield
Hampshire	Northampton
Worcester	Milford
Worcester North	Fitchburg

Fall sessions begin this month; details of the program are listed below. Programs for the winter and spring courses will be printed prior to the opening sessions. Printed programs with complete information will be mailed to every registered physician before the courses begin.

These courses are sponsored by the Massachusetts Medical Society in co-operation with the Massachusetts Department of Public Health, the United States Public Health Service and the Federal Children's Bureau. Registration is free to all legally registered physicians of the Commonwealth. For further information the district chairman of postgraduate instruction should be consulted.

The programs for the fall sessions are as follows:

Barnstable District: Hyannis

SUBJECT	DATE
Recent Advances in Medical Therapeutics: Sedatives; analgesics; cathartics; sulfanilamide compounds; dangerous drugs	October 27
Dermatitis and Eczema (see below)	November 3
Chemotherapy in the Treatment of Gonococcal Infection	November 10
Pediatric Case Discussions	November 17
Technic and Treatment of Primary, Secondary and Tertiary Syphilis	November 24
Operative Obstetrics: Indications and technic	December 1
Management of Abdominal Distention	December 8
Obstetric Complications, with Case Histories and Clinical Problems	December 15

Meetings to be held at the Cape Cod Hospital, Hyannis, Sundays, at 4:00 p.m.

Donald E. Higgins, M.D., *Chairman*
Main Street, Cotuit

Bristol North District: Taunton

SUBJECT	DATE
Infections of the Hands and Feet	October 24
Obstetric Complications, with Case Histories and Clinical Problems	October 31
Pediatric Case Discussions	November 7
Acute Abdominal Pain: Its interpretation and management	November 14
Therapeutic Uses of Preparations of Endocrine Glands: Thyroid gland, pituitary gland, ovary, testis and adrenal cortex	November 21
Dermatitis and Eczema (see below)	December 5
Technic and Treatment of Primary, Secondary and Tertiary Syphilis	December 12
Gonococcal Infections in the Armed Forces and the Civilian Population	December 19

Meetings to be held at the Morton Hospital, Taunton, Thursdays, at 4:00 p.m.

Lester E. Butler, M.D., *Chairman*
148 High Street, Taunton

Note: Because of the holiday, the course will be omitted November 28.

Bristol South District: New Bedford

SUBJECT	DATE
Gonococcal Infections in the Armed Forces and the Civilian Population	October 25
Diagnosis and Treatment of Minor Lesions of Rectum and Anus	November 1
The Clinical Recognition of the Types of Jaundice and Recent Advances in Their Treatment	November 8
The Treatment of Varicose Veins	November 15
Pediatrics (subject to be announced)	November 22
Acute Abdominal Pain: Its interpretation and management	November 29
Technic and Treatment of Primary, Secondary and Tertiary Syphilis	December 6
Operative Obstetrics: Indications and technic	December 13

Meetings to be held at St. Luke's Hospital, New Bedford, Fridays, at 4:00 p.m.

Robert H. Goodwin, M.D., *Chairman*
286 Pleasant Street, New Bedford

Essex North District: Lawrence

SUBJECT	DATE
Diagnosis, Treatment and Prognosis of Central-Nervous-System Syphilis	October 25
Therapeutic Uses of Preparations of Endocrine Glands: Thyroid gland, pituitary gland, ovary, testis and adrenal cortex	November 1
Management of Abdominal Distention	November 8
Obstetric Complications, with Case Histories and Clinical Problems	November 15
Infections of the Hands and Feet	November 22
Pediatric Case Discussions	November 29
Chemotherapy in the Treatment of Gonococcal Infection	December 6
Dermatitis and Eczema (see below)	December 13

Meetings to be held at the Clover Hill Hospital, 161 Berkeley Street, Lawrence, Fridays, at 4:30 p.m.

John Parr, M.D., *Chairman*
7 Hampshire Street, Methuen

Essex South District: Salem

SUBJECT	DATE
Operative Obstetrics: Indications and technic	October 22
Pediatric Case Discussions	October 29
Technic and Treatment of Primary, Secondary and Tertiary Syphilis	November 5
Nutritional Deficiencies and the Uses of Preparations of Vitamins	November 12
Diagnosis and Treatment of Minor Lesions of Rectum and Anus	November 19
Chemotherapy in the Treatment of Gonococcal Infection	November 26
Management of Abdominal Distention	December 3
Recent Advances in Medical Therapeutics: Sedatives; analgesics; cathartics; sulfanilamide compounds; dangerous drugs	December 10

Meetings to be held in the Conference Room, Salem Hospital, Tuesdays, at 4:00 p.m.

J. Robert Shaughnessy, M.D., *Chairman*
24½ Winter Street, Salem

Middlesex North District: Lowell

SUBJECT	DATE
Diagnosis and Treatment of Minor Lesions of Rectum and Anus	October 25

Chemotherapy in the Treatment of Gonococcal Infection	November 1
Problems in Bronchoscopy	November 8
Recent Advances in Medical Therapeutics: Sedatives; analgesics; cathartics; sulfanilamide compounds; dangerous drugs	November 15
Operative Obstetrics: Indications and technic	November 22
Technic and Treatment of Primary, Secondary and Tertiary Syphilis	November 29
Pediatric Case Discussions	December 6
The Treatment of Varicose Veins	December 13

Meetings to be held at St. John's Hospital, Lowell, Fridays, at 5:00 p.m.

William S. Lawler, M.D., *Chairman*
53 Central Street, Lowell

PLYMOUTH DISTRICT: BROCKTON

SUBJECT	DATE
Nutritional Deficiencies and the Uses of Preparations of Vitamins	October 22
The Treatment of Varicose Veins	October 29
Chemotherapy in the Treatment of Gonococcal Infection	November 5
Pediatric Case Discussions	November 12
Technic and Treatment of Primary, Secondary and Tertiary Syphilis	November 19
Hemorrhage in Pregnancy, Labor and the Puerperium: Its diagnosis and treatment	November 26
Recent Advances in Medical Therapeutics: Sedatives; analgesics; cathartics; sulfanilamide compounds; dangerous drugs	December 3
Diagnosis and Treatment of Minor Lesions of Rectum and Anus	December 10

Meetings to be held in the Nurses' Home of the Brockton Hospital, Tuesdays, at 4:30 p.m.

Walter H. Pulsifer, M.D., *Chairman*
26 Park Avenue, Whitman

The following questions will be discussed in the course on dermatitis and eczema:

Is there such a thing as eczema?

Is allergy fact or fiction?

Are skin tests of value in dermatology?

Are fungous infections (athlete's foot) as prevalent as we are led to believe?

With the diagnosis made, what should be the treatment of common cutaneous eruptions?

DEATHS

HARMER — TORR W. HARMER, M.D., of Winchester, died October 2. He was in his sixtieth year.

Born in Somerville, he attended the local schools and Harvard College, receiving his degree from Harvard Medical School in 1907. He served as surgical house officer at the Massachusetts General Hospital, house physician at the Boston Lying-in Hospital and assistant surgeon at the Infants' Hospital and the Children's Hospital. Dr. Harmer was a consulting surgeon at the Massachusetts Eye and Ear Infirmary and at the Somerville, Winchester, Symmes Arlington and Waltham hospitals.

He was a member of the staff of the Harvard Medical School for many years, having been assistant in surgery and instructor in anatomy. At the time of his death he held the position of instructor in anatomy.

A fellow of the Massachusetts Medical Society and the American Medical Association, he was also a member of the American Association for the Surgery of Trauma, the American College of Surgeons, the American Board of Surgery and the New England Surgical Society. His affiliations included the Aesculapian and Lancet clubs, of Boston.

His widow, a daughter, a son and a sister survive him.

JACKSON — HENRY JACKSON, M.D., of Chestnut Hill, died October 4. He was in his eighty-third year.

Born in Boston he attended the Hopkinson School and Harvard College and received his degree from Harvard Medical School in 1884. He served his internship at the Massachusetts General Hospital, after which he spent a year in Europe, studying at Vienna. From 1886 to 1916 he was a staff member of the Boston City Hospital, eventually becoming physician-in-chief. Dr. Jackson also served as an instructor in clinical medicine at the Harvard Medical School.

He was a member of the Massachusetts Medical Society, the American Medical Association and the Association of American Physicians.

His daughter, Mrs. Kennard Winsor, and a son, Dr. Henry Jackson, Jr., survive him.

SWAN — LAURENCE C. SWAN, M.D., of Beverly, died October 2. He was in his sixtieth year.

Born in Stoughton, he attended Dartmouth College and received his degree from Harvard Medical School in 1907. Shortly after graduation he settled in Beverly, where he practiced for over thirty-one years. Dr. Swan was a fellow of the Massachusetts Medical Society and the American Medical Association.

His widow, a daughter, a son and a brother survive him.

VILLONE — ANTHONY J. VILLONE, M.D., of Quincy, died October 6. He was in his fiftieth year.

Dr. Villone attended Fordham University and received his degree from Tufts College Medical School in 1918. He then enlisted in the Medical Corps of the United States Navy, and was a retired lieutenant. Dr. Villone was a member of the Massachusetts Medical Society and the American Medical Association.

His widow, parents, two sisters and two brothers survive him.

CORRESPONDENCE

RESULTS OF MARCH, 1940, BOARD EXAMINATIONS

To the Editor: I am enclosing a statement of the results of the March, 1940, examination conducted by the Board of Registration in Medicine.

STEPHEN RUSHMORE, M.D., *Secretary.*

State House, Boston

School	First Time		Second or Third Times		Fourth or More Times		Total		Total Applicants
	Passed	Failed	Passed	Failed	Passed	Failed	Passed	Failed	
Boston University School of Medicine*	2						2		2
College of Physicians and Surgeons (Boston)	1		2	10		3	3	13	16
Harvard Medical School*	6						6		6
Massachusetts College of Osteopathy†	1		7	8			8	8	16
Middlesex University School of Medicine	2	7	18	21	3	6	23	34	57
Tufts College Medical School*	9						9		9
Baylor University College of Medicine*			1				1		1
Chicago College of Osteopathy†				1				1	1
Chicago Medical School	1						1		1
College of Medical Evangelists*			1				1		1
George Washington University School of Medicine*	2						2		2
Georgetown University School of Medicine*			1				1		1
Hahnemann Medical College and Hospital of Philadelphia*	1						1		1
Indiana University School of Medicine*	1						1		1
Jefferson Medical College of Philadelphia*	1						1		1
Johns Hopkins University School of Medicine*	2						2		2
Kansas City University of Physicians and Surgeons		1	2	7	1	5	3	13	16
Kirksville College of Osteopathy and Surgery†			4	1		2	4	3	7
Mid-West Medical College			3	1	2	3	5	4	9
Philadelphia College of Osteopathy†			1	1	2		3	1	4
St. Louis College of Physicians and Surgeons				1				1	1
Tulane University of Louisiana School of Medicine*	1						1		1
University of Cincinnati College of Medicine*	1						1		1
University of Illinois College of Medicine*	1						1		1
University of Minnesota Medical School*	1						1		1
University of Tennessee College of Medicine*	1						1		1
University of Rochester School of Medicine*	1						1		1
University of Virginia Department of Medicine*	1	1					1	1	2
University of Wisconsin Medical School*	1						1		1
Albert University*	1						1		1
Elizabeth University*			1				1		1
McGill University*	3						3		3
Royal University, Hungary*	1						1		1
University of Basle*		1						1	1
University of Berlin*	2			1			2	1	3
University of Bern*	2						2		2
University of Bologna*	1		1				2		2
University of Breslau*	5						5		5
University of Edinburgh*			1				1		1
University of Frankfort*	2						2		2
University of Freiburg*	1						1		1
University of Hamburg*				1				1	1
University of Heidelberg*	2						2		2
University of Koenigsberg*	1		1				2		2
University of Lausanne*	1				1		2		2
University of Leipzig*	1						1		1
University of Milan*	3						3		3
University of Montreal*	1						1		1
University of Munich*	4						4		4
University of Naples*			1	1			1	1	2
University of Paris*			1				1		1
University of Prague*	3		1				4		4
University of Tartu (Estonia)*						1		1	1
University of Vienna*	21	1	1				22	1	23
	92	11	48	54	9	20	149	85	234

*Approved schools.
†Osteopathic schools.

Approved schools	87	3‡	11	3‡	1	1‡	99	7‡	106
Non-approved schools	4	8	25	40	6	17	35	65	100
Osteopathic schools	1		12	11	2	2	15	13	28
	92	11	48	54	9	20	149	85	234

‡The exponents represent graduates of European schools.

COMMITTEE FOR THE DEFENSE OF MEDICAL RIGHTS

To the Editor: The Executive Committee of the Committee for the Defense of Medical Rights has issued a statement in support of an initiative petition to amend the Massachusetts laws relating to the prevention of pregnancy. The petition, which would allow physicians to provide medical contraceptive information and care to married persons for the protection of life or health, and which was filed with the Secretary of State on September 4, was signed by the following citizens of Massachusetts: Karl T. Compton, Sarah T. Curwood, Robert G. Dodge, Frederick M. Eliot, Nathaniel W. Faxon, M.D., Frederick C. Irving, M.D., William R. Manchester, Mary Pratt Potter, John Rock, M.D., and Curtis C. Tripp, M.D.

In the initiative petition the Legislature is asked to amend Sections 20 and 21 of Chapter 272 of the General Laws by adding at the end thereof the following:

> The provisions of this section and of section twenty which relate to the prevention of pregnancy and the prevention of conception shall not apply to treatment or prescription given to married persons for protection of life or health by or under the direction of physicians registered in accordance with the provisions of Chapter 112; nor to teaching in chartered medical schools; nor to publication or sale of medical treatises or journals.

The statement issued by the Executive Committee reads as follows:

> The initiative petition proposed is for a bill to ensure to physicians the right to protect the life, health and reason of married persons when these might be endangered by pregnancy. It is designed to prevent the legal interference with this phase of the practice of medicine, which has only recently resulted from the enforcement of an old Massachusetts statute.
>
> The principle of legal freedom for physicians to provide contraceptive medical care to married women whose physical or mental condition would suffer by pregnancy or who could be expected to produce only seriously defective individuals has been approved by the American Medical Association, and by many other medical and religious bodies.
>
> Support of this petition does not imply support of either the methods or philosophy of "birth control." It means only support of the principle of freedom in the licensed teaching and practice of medicine.
>
> The initiative petition is so designed as to protect marital security and to bring under licensed control the present, widespread bootleg traffic in contraceptive information and material.

Under the constitutional procedure laid down for the presentation of initiative petitions to the Legislature, 20,000 signatures of registered Massachusetts voters, certified by the registrars of voters of the cities and towns of their respective residences, must be appended to this petition and filed with the Secretary of State by December 4 of this year. It is understood that 40,000 signatures will actually be sought by November 8, in order to be assured of fulfilling the legal requirements, and in order to have time for certification and checking of signatures before the December 4 deadline.

The Secretary of State will transmit the initiative petition to the 1941 Legislature, which convenes in January. It will then be referred to the proper committee for public hearings, and reported to the Legislature, where a recorded vote is required by law on or before the first Wednesday in June. If the Legislature does not enact the proposed amendment, 5000 additional signatures of registered voters may be obtained between the first Wednesday in June and the first Wednesday in August, to be filed with the Secretary of State by the latter date. The question will then be submitted to the voters as a referendum in November, 1942.

Physicians who wish to aid in obtaining signatures to the initiative petition may obtain blanks by getting in touch with Somers H. Sturgis, M.D., Secretary, Committee for the Defense of Medical Rights, 270 Commonwealth Avenue, Boston.

WILLIAM H. ROBEY, M.D., *President,*
Executive Committee,
Committee for the Defense of Medical Rights.

270 Commonwealth Avenue,
Boston.

NOTICES

BOSTON DOCTORS' SYMPHONY ORCHESTRA

The Boston Doctors' Symphony Orchestra will rehearse under Alexander Thiede, former concertmaster with the Cleveland Symphony Orchestra, every Thursday at 8:30 p.m. Those interested in becoming members should communicate with Dr. Julius Loman, Pelham Hall Hotel, Brookline (BEA 2430).

PETER BENT BRIGHAM HOSPITAL

Weekly clinicopathological conferences will be held in the amphitheater on Mondays from 12:15 to 1:15.

Weekly clinicoroentgenological conferences will be held every Tuesday in the amphitheater between 12:15 and 1:15.

SUFFOLK DISTRICT MEDICAL SOCIETY

The 1940–1941 program of the Suffolk District Medical Society contains certain innovations, the most important being a noon luncheon meeting. Three meetings, rather than five as in previous years, will be held. The fall meeting will be the stated meeting, the midwinter the scientific meeting and the spring the annual meeting.

PROGRAM

Stated Meeting. Wednesday, October 30. Hotel Somerset.
- 12:00 m. Luncheon for those members who indicate their desire to be present.
- 12:45 p.m. Business meeting.
- 1:00 p.m. "Lessons for Physicians and Surgeons from the Army and Navy." Speakers to be announced.

Scientific Meeting. Wednesday, January 29. Boston Medical Library.
- 8:15 p.m. "Sedatives, Hypnotics and Anesthetics." Speakers to be announced.

Annual Meeting. Wednesday, April 30. Boston Medical Library.
- 8:15 p.m. "Symposium on the Toxemias of Pregnancy." To be arranged by Dr. Raymond S. Titus.

MASSACHUSETTS MEMORIAL HOSPITALS

There will be a staff meeting of the Massachusetts Memorial Hospitals in the Evans Memorial Auditorium on Friday, October 25, at 8:15 p.m. Dr. Chester S. Keefer will be the chairman.

PROGRAM

Current Concepts of the Pathologic Physiology of Hypertension. Dr. Robert W. Wilkins. Discussion by Drs. Reginald H. Smithwick and James P. O'Hare.

Roentgenologic Aspects of the Heart in Hypertension. Dr. George Levene. Discussion by Dr. Merrill Sosman.

PETER BENT BRIGHAM HOSPITAL

A joint medical and surgical clinic at the Peter Bent Brigham Hospital will be held on Wednesday, October 16, from 2 to 4 p.m. Drs. C. S. Burwell and H. F. Newton will speak on "Dyspnea and Cough." A clinicopathological conference, conducted by Dr. Elliott C. Cutler, will take place from 4 to 5 p.m.

Physicians and students are cordially invited to attend.

NEW ENGLAND PATHOLOGICAL SOCIETY

The next meeting of the New England Pathological Society will be held in the amphitheater (Vila Street) of the Boston Children's Hospital on Thursday evening, October 17, at 8:15.

PROGRAM

Macrogenitosomia Praecox Associated with Hypothalamic Tumors. Dr. Robert E. Gross.

Natural Vital Staining of Teeth of the New Born. Dr. Paul E. Boyle.

Marble Bones. Dr. Albert Frank.

Schüller–Christian's Disease and Allied Disorders. Dr. Sidney Farber.

An exhibit illustrating some of the research activities of the Department of Pathology of the Children's Hospital (Shattuck Street entrance), and specimens of interest selected from routine surgical and autopsy material will be on display, from 7:00 to 8:15 and again after the meeting.

NEW ENGLAND WOMEN'S MEDICAL SOCIETY

The fall meeting of the New England Women's Medical Society will be held at the Myles Standish Hotel on Thursday, October 17, at 7:00 p.m. Dr. Timothy Leary will speak, his subject being "Some Experiences of a Medical Examiner."

ST. PAUL'S CATHEDRAL

A special service will be held at St. Paul's Cathedral, Tremont Street, Boston, on Sunday evening, October 20, at 7:00. Dr. Nathan B. Van Etten, president of the American Medical Association, will speak, the title of his address being "Medical Horizons." All doctors, nurses and medical students are cordially invited.

NEW ENGLAND SOCIETY OF PHYSICAL MEDICINE

The regular monthly meeting of the New England Society of Physical Medicine will be held on Wednesday evening, October 16, at the Hotel Kenmore, Boston.

The council will meet at 6:00, and an informal dinner will be held in the Empire Room at 6:30. At 8:00, Mr. Robert D. Beaird, technical engineer of General Electric X-ray Corporation, Chicago, will speak on the subject, "Medical Electrophysics."

All members of the medical profession are cordially invited to attend.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING SUNDAY, OCTOBER 13

MONDAY, OCTOBER 14

12:15–1:15 p.m. Clinicopathological Conference. Peter Bent Brigham Hospital amphitheater.

TUESDAY, OCTOBER 15

*9–10 a.m. Steroid Hormone Excretion Rates Associated with Dysmenorrhea. Drs. N. T. Werthessen and R. E. Brownlee. Joseph H. Pratt Diagnostic Hospital.

*12 m. The Diagnosis and Treatment of Pulmonary Bleeding. Dr. Moses J. Stone. South End Medical Club. Headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston.

12:15–1:15 p.m. Clinicoroentgenological conference. Peter Bent Brigham Hospital amphitheater.

WEDNESDAY, OCTOBER 16

*9–10 a.m. Hospital case presentation. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

*12 m. Clinicopathological conference. Children's Hospital.

*2–4 p.m. Dyspnea and Cough. Drs. C. S. Burwell and H. F. Newton. Joint medical and surgical clinic. Peter Bent Brigham Hospital.

*8 p.m. Medical Electrophysics. Mr. Robert D. Beaird. New England Society of Physical Medicine. Hotel Kenmore, Boston.

THURSDAY, OCTOBER 17

*9–10 a.m. Nephritic Clinic. Dr. R. W. Buck. Joseph H. Pratt Diagnostic Hospital.

7 p.m. Some Experiences of a Medical Examiner. Dr. Timothy Leary. New England Women's Medical Society. Myles Standish Hotel, Boston.

8:15 p.m. New England Pathological Society. Boston Children's Hospital amphitheater (Vila Street).

FRIDAY, OCTOBER 18

*9–10 a.m. Recent Advances in Anesthesiology. Dr. F. W. Marvin. Joseph H. Pratt Diagnostic Hospital.

SATURDAY, OCTOBER 19

*9–10 a.m. Hospital case presentation. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

*Open to the medical profession.

OCTOBER 11, 12 — Pan-American Congress of Ophthalmology. Page 898, issue of May 23.

OCTOBER 14–25 — 1940 Graduate Fortnight of the New York Academy of Medicine. Page 305, issue of August 22.

OCTOBER 16 — Waltham Medical Meeting. Page 557, issue of October 3.

OCTOBER 20 — St. Paul's Cathedral. Notice above.

OCTOBER 21 — American Board of Internal Medicine. Page 369, issue of February 29.

OCTOBER 25 — Staff meeting, Massachusetts Memorial Hospitals. Notice above.

NOVEMBER 13, 14 — New England Postgraduate Assembly. Cambridge, Massachusetts.

NOVEMBER 14 — Pentucket Association of Physicians. Page 263, issue of August 15.

DECEMBER 27–29 — National Convention of the Association of Medical Students, Boston.

JANUARY 4, 1941 — American Board of Obstetrics and Gynecology. Page 1064, issue of June 20.

MARCH 8 — American Board of Ophthalmology. Page 201, issue of August 1.

APRIL 21–25 — American College of Physicians. Page 1065, issue of June 20.

JUNE 2–6 — American Medical Association. Cleveland, Ohio.

DISTRICT MEDICAL SOCIETIES

SUFFOLK

OCTOBER 30 — Page 604.

NOVEMBER 7 — Censors' meeting. Page 305, issue of August 22.

JANUARY 29 — Page 604.

APRIL 30 — Page 604.

WORCESTER

November 13 — Grafton State Hospital, Grafton.
December 11 — St. Vincent Hospital, Worcester.
January 8, 1941 — Worcester City Hospital, Worcester.
February 12 — Worcester State Hospital, Worcester.
March 12 — Memorial Hospital, Worcester.
April 9 — Hahnemann Hospital, Worcester.

Supper will be served at 6:30 p.m. followed by a business meeting and scientific program.

BOOK REVIEWS

The Electrocardiogram in Congenital Cardiac Disease. By Maurice A. Schnitker, B.Sc., M.D. 8° cloth, 147 pp., with 24 plates. Cambridge, Massachusetts: Harvard University Press, 1940. $3.00.

The clinical recognition of certain patterns of congenital heart disease has come from a relatively recent correlation of the work of the practitioner and the pathologist. One aid to the clinician has been the electrocardiograph, but until the appearance of this book, the recorded experience in electrocardiography in proved cases of congenital heart disease has never been adequately reviewed and collected. The analysis of the data on which the book is based must have been a bewildering task because of the multiplicity of combined anomalies in so many of the cases and the difficulty in allocating the preponderant total cardiac effect to the principal lesion. A discussion of the physiology of the various anomalies provides an excellent basis for understanding the strains peculiar to specific regions in the heart and great vessels. One hundred and nine cases are reported, one hundred and six with autopsy, and one proved by surgical operation. The electrocardiograms are reproduced in one hundred and eight cases. The normal electrocardiogram in childhood is described first, and the congenital anomalies then considered in the acyanotic, late cyanotic and cyanotic groups. The author states: "With most lesions there is no specificity of electrocardiographic curves in a given group of similar cases. Group specificity was encountered only in congenital heart block, in dextrocardia with reversed chambers — either alone or as a part of generalized situs viscerum inversus — and in tricuspid valve disease, particularly tricuspid stenosis." However, correlations do occur often enough to be very significant in the diagnosis of other important groups.

The book will serve as a valuable reference work in determining the probable lesions in puzzling cases. The reviewer agrees with the author's statement, "The more refined and exact the diagnosis, the more accurately can we prognosticate, and the more intelligent will be our management of the patient with the malformed heart."

Diverticula and Diverticulitis of the Intestine. By Harold C. Edwards, M.S., London, F.R.C.S., Eng. 8°, cloth, 335 pp., with 223 illustrations, many in color. Baltimore: Williams & Wilkins Company, 1939. $8.00.

The author of this interesting and excellent treatise on diverticulosis and diverticulitis of the intestine has presented in a clear-cut and forceful manner a subject which should be interesting to the surgeon and the internist alike. He considers such conditions in the duodenum and continues down the intestinal tract to the rectum. His opinions regarding the etiology and the pathology of diverticulosis and diverticulitis are well thought out. Indeed, this phase of the subject is presented in the most logical manner that the reviewer has yet seen. In particular, his explanation of the method of development from the earliest stage of a diverticulum of the colon is well worth reading, and his drawings and photographs illustrate each phase distinctly.

The treatment of diverticulosis and diverticulitis occurring in different parts of the intestinal tract, as advocated by the author, is sound and conservative. A few minor exceptions might be taken to his medical management of diverticulosis of the colon, but these are of little significance.

Taken as a whole, the book is useful and readable; it deserves a place in modern medical literature.

Elmer and Rose Physical Diagnosis. Harry Walker, M.D. Eighth edition. 8°, cloth, 792 pp., with 295 illustrations. St. Louis: C. V. Mosby Company, 1940. $8.75.

Any text which reaches its eighth edition must have merit. Dr. Walker's revision brings this old favorite fairly well up to date, and the book takes its place beside Cabot and Adams, Emerson, Sutton and the other comprehensive textbooks of physical diagnosis. The reviewer personally prefers to use a smaller, epitomized handbook for teaching purposes. A truly exhaustive monograph, such as that of Edens in German, is still lacking in English.

A few minor criticisms may be mentioned. Orthopercussion is incorrectly defined (page 222); "torsus" palatinus is correctly "torus" palatinus (page 72); it is questionable whether a detailed discussion of polygraphy any longer has a place in a textbook, since the procedure is certainly no longer in common use (pages 743-752); finally, the technic of joint examination is generally inadequate.

The book is printed on gray-blue tinted paper. This adversely affects its appearance, but may be restful to the student's eyes.

Doctors in Shirt Sleeves; Musings on Hobbies, Meals, Patients, Sport and Philosophy. Edited by Sir Henry Bashford. 8°, cloth, 294 pp. New York: Veritas Press, 1940. $2.50.

For a number of years, the *Lancet* has published a column written by physicians, entitled "Grains and Scruples." The material now appears in book form, printed in Great Britain, but issued with a New York imprint. These papers were contributed by various members of the British medical profession on any subject that they desired. Most of them relate to physicians, their patients, their hobbies and their memories of the past. The articles tend to be philosophical essays, and as such are of considerable interest to the medical profession in general. Some are factual, such as the article by Squire Sprigge, on "Some Forgotten Medical Journal." Others treat on "The Biology of War," "Science and Spiritual Values," "Some Old Days in India," "On Hobbies" and "The Life of a Surgeon." There is something of interest in this volume for every reader. The papers naturally vary in both style and quality. The book would form a pleasing gift for a physician and would give him a few hours of pleasant relaxation.

Attaining Womanhood. By George W. Corner, M.D. 8°, paper, 92 pp. New York: Harper & Bros., 1939. $1.00.

This little book is a companion volume to the author's similar book for boys, *Attaining Manhood.* A most satisfactory book in every way, it is well illustrated with simple, clear drawings emphasizing the various phases of reproduction. It undoubtedly is one of the best books for young girls to read and study.